

(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

EP 1 300 396 A1

(12)

EUROPEAN PATENT APPLICATION

published in accordance with Art. 158(3) EPC

(43) Date of publication:
09.04.2003 Bulletin 2003/15

(51) Int Cl.7: C07D 213/71

(21) Application number: 01936920.6

(86) International application number:
PCT/JP01/04857

(22) Date of filing: 08.06.2001

(87) International publication number:
WO 01/096308 (20.12.2001 Gazette 2001/51)

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE TR
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: 12.06.2000 JP 2000175966
13.09.2000 GB 0022483

(71) Applicant: Eisai Co., Ltd.
Tokyo 112-8088 (JP)

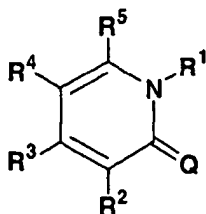
(72) Inventors:
• NAGATO, Satoshi
Matsudo-shi, Chiba 271-0076 (JP)
• UENO, Kohshi
Tsukuba-shi, Ibaraki 305-0042 (JP)
• KAWANO, Koki
Tsukuba-shi, Ibaraki 305-0045 (JP)
• NORIMINE, Yoshihiko
Tsukuba-shi, Ibaraki 305-0061 (JP)
• ITO, Koichi
Abiko-shi, Chiba 270-1143 (JP)
• HANADA, Takahisa
Tsukuba-shi, Ibaraki 305-0003 (JP)

- UENO, Masataka
Kitasouma-gun, Ibaraki 302-0121 (JP)
- AMINO, Hiroyuki
Tsukuba-shi, Ibaraki 305-0821 (JP)
- OGO, Makoto
Tsukuba-shi, Ibaraki 305-0035 (JP)
- HATAKEYAMA, Shinji
Tsukuba-shi, Ibaraki 305-0035 (JP)
- URAWA, Yoshio
Kashima-shi, Ibaraki 314-0031 (JP)
- NAKA, Hiroyuki
Tsukuba-shi, Ibaraki 305-0035 (JP)
- GROOM, Anthony, John
Swindon, Wiltshire SN1 2PX (GB)
- RIVERS, Leanne
Tonbridge, Kent TN12 0SE (GB)
- SMITH, Terence
Cambridge, Cambridgeshire CB1 2LE (GB)

(74) Representative:
Cornish, Kristina Victoria Joy et al
Kilburn & Strode,
20 Red Lion Street
London WC1R 4PJ (GB)

(54) 1,2-DIHYDROPYRIDINE COMPOUNDS, PROCESS FOR PREPARATION OF THE SAME AND USE THEREOF

(57) The present invention provides a novel compound having an excellent AMPA receptor inhibitory action and/or kainate inhibitory action. A compound represented by the following formula, a salt thereof or hydrates thereof.



(I)

In the formula, Q indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or a group represented by the formula -X-A (wherein X indicates a single bond, an optionally substituted C₁₋₆ alkylene group etc.; and A indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbonocyclic group or 5- to 14-membered aromatic heterocyclic group etc.).

EP 1 300 396 A1

Description

Field of the Invention

5 **[0001]** The present invention relates to a novel compound, a salt thereof and hydrates thereof, and to a method for manufacturing the same. More specifically, it relates to a pyridone compound, a salt thereof and hydrates thereof which are useful as inhibitors to non-NMDA receptors, particularly to AMPA receptor.

Prior Art

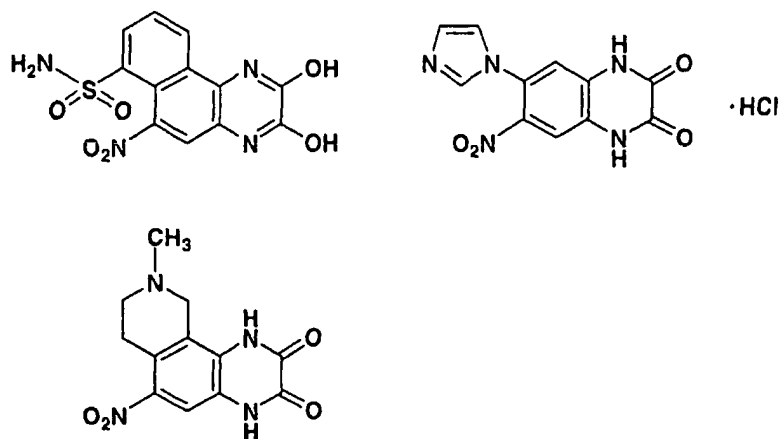
10

[0002] Glutamate and aspartate are important amino acids which participate in nerve functions such as recognition, memory, movement, respiration, cardiovascular adjustment and sensation and are called excitatory neurotransmitters as well. In the expression of their physiological activities, an interaction with a specific receptor is important and, generally, two types of receptors - an ion channel type and a G-protein coupled type - have been known. The former is further classified into N-methyl-D-aspartate (NMDA) receptor, α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor, kainate receptor, etc. On the other hand, the amino acid as an excitatory neurotransmitter has been known to induce neurotoxicity by, for example, abnormal excitation of central nerves. It has been noted that the said toxicity is as serious as being accompanied by the death of nerve cells causing various nervous diseases. Main nervous diseases which have been known are cerebral ischemia, head injury, spinal cord injury, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), Huntington's chorea, AIDS nervous disturbance, epilepsy, neurodegeneration observed after the state of hypoxia, mental disorder, mobility disturbance, pain, spasticity, nervous disturbance by toxin in food, various neurodegenerative diseases, various mental diseases, chronic pain, migraine, cancer pain and pain caused by diabetic nervous disturbance. They are serious diseases where many mechanisms of onset, etc. have not been clarified yet and pharmaceutical agents which are effective for the therapy have not been found yet but it is believed that they are closely related to excessive release/accumulation of excitatory neurotransmitters, changes in expressing pattern of receptors, etc. For example, it has been reported that glutamate concentration in cerebrospinal fluid and plasma increases in stroke, cerebral ischemia, head injury and spinal cord injury (Castillo, J., Dazalos, A. and Noya, M., *Lancet*, 1997, 346:79-83; etc.). There is a report that neuropathy occurs when glutamate, NMDA, AMPA, kainate, etc. are excessively applied to nerve cells (Meldrum, B., *Brain Res. Reviews*, 18, 293, 1993). There are reports that, in Alzheimer's disease, β -amyloid protein enhances the neurotoxicity of glutamate and that it promotes the release of glutamate (Arias, C., Arrieta, I. and Tapia, R., *J. Neurosci. Res.*, 1995, 41:561-566; etc.). In the case of Parkinson's disease, there are reports that L-dopa hydroxide activates the AMPA receptor (Cha, J. J., et. al., *Neurosci. Lett.*, 1991, 132:55-58) and enhances the neurotoxicity (Olney, J. W., et. al., 1990, 108:269-272; Rosenberg, P. A., et. al., *Proc. Natl. Acad. Sci. USA*, 1991, 88:4865-4869). There is another report that L-dopa promotes the generation of free radicals resulting in a rise of oxidative stress (Smith, T. S., et. al., *Neuroreport*, 1994, 5:1009-1011). In the case of Huntington's chorea, it is reported that a substance which inhibits the release of glutamate is effective in improving the symptoms. In the case of ALS, there are many reports showing the participation of glutamate in its pathology. There are some cases where the AIDS patients suffer from recognition nerve function deficiency and, even in such a nerve disease, participation of glutamate is suggested. For example, it is reported that gp 120 which is a glycoprotein in an envelope of HIV virus suppresses the uptake of glutamate by astrocytes (Dreyer, E. B., *Eur. J. Neurosci.*, 1995, 7:2502-2507; Ushijima, H., et. al., *Eur. J. Neurosci.*, 1995, 7:1353-1359) while a substance which inhibits the release of glutamate suppresses the neurodegeneration by gp 120 (Sindou, P., et. al., *J. Neurosci.* 1994, 126:133-137; Muller, W. E. G., et. al., *Eur. J. Pharmacol. Molec. Pharmacol.*, 1992, 226:209-214; Lipton, S. A., *Neurology*, 1992, 42:1403-1405). With regard to allergic encephalomyelitis, there is a report that, in the mice where the said inflammation takes place, enzyme which decomposes glutamate incorporated from outside of cells is deficient (Hardin-Pouzet, H., *Glia*, 1997, 20:79-85). Olivopontocerebellar atrophy is a disease which is sometimes combined with Parkinson's disease and an antibody to GluR2 which is a subunit constituting the AMPA receptor has been found (Gahring, L. C., *Neurology*, 1997, 48:494-500) and the relation between olivopontocerebellar atrophy and AMPA receptor is suggested. With regard to a report for epilepsy, it is reported that, in the mice which are unable to construct the GluR2 in AMPA receptor, Ca^{2+} permeability of the AMPA receptor increases whereby it is apt to cause a sudden onset resulting in death (Brusa, R., *Science*, 1995, 270:1677-1680). Besides the above, it is reported that NBQX (2,3-dihydroxy-6-nitro-7-sulfamoylbenz [f] quinoxaline; Sheardown, et al., *Science*, 247, 571, 1990) and other inhibiting compounds to AMPA receptors have antianxiety and anticonvulsant action (*J. Pharmacol. Exp. Ther.*, 260, 742, 1992; *Pharmacol. Biochem. Behavior*, 1998, 60:119-124) and there are also reports for the connection of AMPA receptor/kainate receptor with urinary disturbance, drug abuse, pain, etc. (*J. Pharmacol. Exp. Ther.*, 280, 894-904, 1997; *Neuroscience Letters*, 268:127-130, 1999).

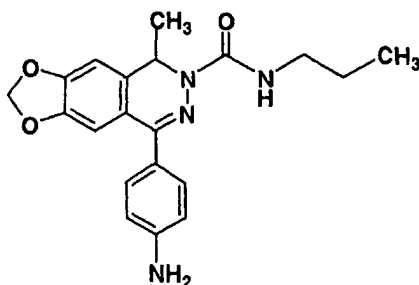
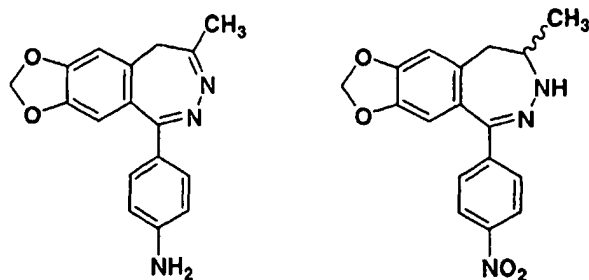
[0003] It can be expected that the substances showing an antagonistic action to excitatory neurotransmitter receptors are useful for the therapy of the above-mentioned nerve diseases. At present, the usefulness of the substances having

an antagonistic action to non-NMDA receptors such as AMPA receptor and kainate receptor is particularly expected. For example, it is reported that inhibitors of the interaction of glutamate with the AMPA and/or kainate receptor complex are useful in treating demyelinating disorders such as encephalitis, acute disseminated encephalomyelitis, acute demyelinating polyneuropathy (Guillain Barre syndrome), chronic inflammatory demyelinating polyneuropathy, multiple sclerosis, Marchifava-Bignami disease, central pontine myelinolysis, Devic syndrome, Balo disease, HIV- or HTLV-myelopathy, progressive multifocal leucoencephalopathy, a secondary demyelinating disorder; for example, CNS lupus erythematodes, polyarteritis nodosa, Sjogren syndrome, sarcoidosis, isolated cerebral vasculitis, etc. as secondary demyelinating disorders, etc. in WO00/01376. With regard to the compound having an inhibitory action to AMPA receptor and kainate receptor, there are reports for the following compounds for example.

(1) Competitive AMPA receptor-inhibiting compounds represented by the following formulae.

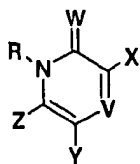


(2) Non-competitive AMPA receptor-inhibiting compounds represented by the following formulae.

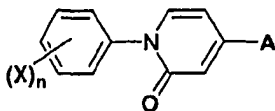


(3) Besides the above, there are reports on competitive AMPA receptor-inhibiting compounds having a quinoxaline-dione skeleton in WO 94/25469, WO 96/10023, US 5356902, etc. and there are reports on non-competitive AMPA receptor-inhibiting compounds in WO 95/01357, WO 97/28135, WO 97/18163, WO 97/43276, WO 97/34878, WO 98/38173, EP 802195, DE 19643037, etc.

[0004] On the other hand, with regard to 1,2-dihydropyridine compounds, there have been several reports for them such as the compounds represented by the formula



[in the formula, R is a hydrogen atom, a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkoxy group, etc.; V is CH or N; W is O or S; X is a phenyl group which is unsubstituted or substituted with one or more group(s) selected from a C₁₋₆ alkyl group, CF₃, a cyano group, a nitro group, halogen, etc. or an aromatic hetero group which is substituted with one or more group(s) selected from a C₁₋₆ alkyl group, CF₃, halogen, etc.; Y is a hydrogen atom, a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, an aryl group, etc.; and Z is halogen, a C₃₋₆ cycloalkyl group, a C₁₋₆ alkylthio group, a C₂₋₆ alkenylthio group, an aryl group, etc.] or salts thereof as a ligand for GABA_A subunit in WO 98/55480 and the compounds represented by the formula



[in the formula, n is 0, 1, 2, 3, 4 or 5; X is a hydrogen atom, a C₁₋₄ alkyl group, a C₁₋₄ alkoxy group, a trifluoromethyl group, a trifluoromethoxy group or halogen; A is an amino group, a C₁₋₄ alkylamino group, a C₁₋₄ dialkylamino group,

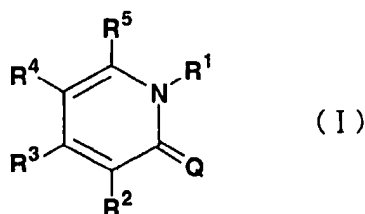
a morpholino group, a piperidino group or a pyrrolidino group] useful for therapy of epilepsy in WO 00/07988 but their connection with AMPA receptor and kainate receptor has not been known at all.

[0005] As such, there has been a brisk demand for the compounds which inhibit AMPA receptor/kainate receptor and are useful as pharmaceutical agents. However, the compounds which exhibit an excellent inhibiting action to AMPA receptor and/or kainate receptor and are highly useful as pharmaceutical agents effectively acting in clinical field have not been found yet. Thus, an object of the present invention is to investigate and find a compound which inhibits AMPA receptor and/or kainate receptor which suppresses the neurotoxicity of excitatory neurotransmitters and achieves an excellent neuroprotective action as pharmaceutical agents being useful as therapeutic/preventing/improving agents for various nerve diseases.

Disclosure of the Invention

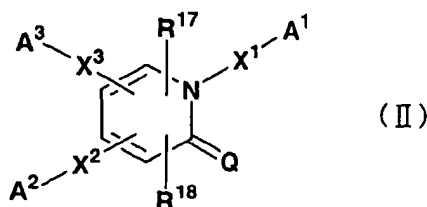
[0006] Under such circumstances, the present inventors have carried out an intensive study and, as a result, they have succeeded in synthesizing a novel compound represented by the formula (I), a salt thereof or hydrates thereof, and have found an excellent method for producing the compound or a salt thereof, and useful intermediate in the method. Further, quite surprisingly, they have found that the above compound (I), a salt or hydrates thereof shows an excellent antagonistic action to AMPA receptor, whereupon the present invention has been accomplished.

[0007] A compound represented by the following formula, a salt thereof or hydrates thereof.



[0008] In the formula, Q indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or a group represented by the formula -X-A (wherein X indicates a single bond, an optionally substituted C₁₋₆ alkylene group an optionally substituted C₂₋₆ alkenylene group, an optionally substituted C₂₋₆ alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicate hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q indicates an integer of 0, 1 or 2 independently); and A indicates a C₃₋₈ cycloalkyl group, a C₃₋₈ cycloalkenyl group, a 5 to 14 membered non-aromatic heterocyclic group, a C₆₋₁₄ aromatic hydrocarbocyclic group, or a 5 to 14 membered aromatic heterocyclic group which may be substituted respectively, provided that 3 groups among R¹, R², R³, R⁴ and R⁵ are always the same as or different from each other and each indicates -X-A; and the residual 2 groups always indicate hydrogen atom, a halogen atom or a C₁₋₆ alkyl group), provided that in the above-mentioned definition, the cases where (1) Q is O; R¹ and R⁵ are hydrogen atoms; and R², R³ and R⁴ are phenyl groups, (2) Q is O; R¹ and R⁴ are hydrogen atoms; and R², R³ and R⁵ are phenyl groups, and (3) Q is O; R¹ and R² are hydrogen atoms; and R³, R⁴ and R⁵ are phenyl groups, are excluded.

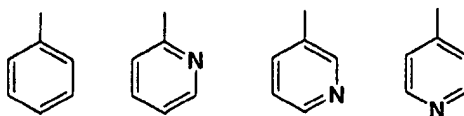
[0009] That is, the present invention relates to (1) the compound represented by the above formula (I), a salt thereof or hydrates thereof; (2) the compound according to the above (1), a salt thereof or hydrates thereof, which is represented by the formula:



wherein Q indicates NH, O or S; X¹, X² and X³ are the same as or different from each other and each indicates a single bond, an optionally substituted C₁₋₆ alkylene group, an optionally substituted C₂₋₆ alkenylene group, an optionally substituted C₂₋₆ alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicate hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q are independent of each other and each indicates an integer of 0, 1 or 2); A¹, A² and A³ are the same as or different from each other and each indicates an optionally substituted C₃₋₈ cycloalkyl group, C₃₋₈ cycloalkenyl group, 5 to 14-membered non-aromatic heterocyclic group, C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group; and R¹⁷ and R¹⁸ are the same as or different from each other and each indicates hydrogen atom, a halogen atom or a C₁₋₆ alkyl group; (3) the compound according to the above (2), a salt thereof or hydrates thereof, wherein X¹, X² and X³ are (1) single bond, (2) a C₁₋₆ alkylene group, a C₂₋₆ alkenylene group or a C₂₋₆ alkynylene group which may be optionally substituted respectively with one or more groups selected from the following substituent group a, (3) -O-, (4) -S-, (5) -CO-, (6) -SO-, (7) -SO₂-, (8) -N(R⁶)-, (9) -N(R⁷)-CO-, (10) -CO-N(R⁸)-, (11) -N(R⁹)-CH₂-, (12) -CH₂-N(R¹⁰)-, (13) -CH₂-CO-, (14) -CO-CH₂-, (15) -N(R¹¹)-S(O)_m-, (16) -S(O)_n-N(R¹²)-, (17) -CH₂-S(O)_p-, (18) -S(O)_q-CH₂-, (19) -CH₂-O-, (20) -O-CH₂-, (21) -N(R¹³)-CO-N(R¹⁴)- or (22) -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ have the same meanings as defined in the above Claim 1); and A¹, A² and A³ are a C₃₋₈ cycloalkyl group, a C₃₋₈ cycloalkenyl group, a 5- to 14-membered non-aromatic heterocyclic group, a C₆₋₁₄ aromatic hydrocarbocyclic group or a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the following substituent group b (the substituent group a: the group consisting of hydroxy group, a halogen atom and nitrile group; and the substituent group b: the group consisting of (1) hydroxy group, (2) a halogen atom, (3) nitrile group, (4) nitro group, (5) a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group or a C₂₋₆ alkynyl group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆ alkylamino group, a di-(C₁₋₆alkyl)amino group, a C₂₋₆ alkenylamino group, a di-(C₂₋₆ alkenylamino) group, a C₂₋₆ alkynylamino group, a di-(C₂₋₆ alkynylamino) group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group, an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, an aralkyloxy group, a TBDMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group, a C₂₋₆ alkenylcarbonyloxy group, a C₂₋₆ alkynylcarbonyloxy group, an N-C₁₋₆ alkylcarbonyl group, an N-C₂₋₆ alkenylcarbonyl group and an N-C₂₋₆ alkynylcarbonyl group, (6) a C₁₋₆ alkoxy group, a C₂₋₆ alkenyloxy group or a C₂₋₆ alkynyloxy group which may be optionally substituted respectively with one or more groups selected from the group consisting of a C₁₋₆ alkylamino group, an aralkyloxy group and hydroxy group, (7) a C₁₋₆ alkylthio group, a C₂₋₆ alkenylthio group or a C₂₋₆ alkynylthio group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆ alkylamino group, an aralkyloxy group, a TBDMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group and a C₁₋₆ alkylcarbonyl group, (8) a carbonyl group substituted with a group selected from the group consisting of a C₁₋₆ alkoxy group, amino group, a C₁₋₆ alkylamino group, a di-(C₁₋₆ alkyl)amino group, a C₂₋₆ alkenylamino group, a di-(C₂₋₆ alkenyl) amino group, a C₂₋₆ alkynylamino group, a di-(C₂₋₆ alkynyl) amino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group and an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, (9) amino group which may be optionally substituted with one or two groups selected from the group consisting of a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkylsulfonyl group, a C₂₋₆ alkenylsulfonyl group, a C₂₋₆ alkynylsulfonyl group, a C₁₋₆ alkylcarbonyl group, a C₂₋₆ alkenylcarbonyl group and a C₂₋₆ alkynylcarbonyl group, (10) a C₁₋₆ alkylsulfonyl group, (11) a C₂₋₆ alkenylsulfonyl group, (12) a C₂₋₆ alkynylsulfonyl group, (13) a C₁₋₆ alkylsulfinyl group, (14) a C₂₋₆ alkenylsulfinyl group, (15) a C₂₋₆ alkynylsulfinyl group, (16) a formyl group, (17) a C₃₋₈ cycloalkyl group or a C₃₋₈ cycloalkenyl group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (18) a 5- to 14-membered non-aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (19) a C₆₋₁₄ aromatic hydrocarbocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, and (20) a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group); (4) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A² and/or A³ are the same as or different from each other and each is an optionally substituted C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl or 5- to 14-membered non-aromatic heteroring; (5) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A² and/or A³ are the same as or different from each other and each is an optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or a 5- to 14-membered aromatic heteroring; (6) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A²

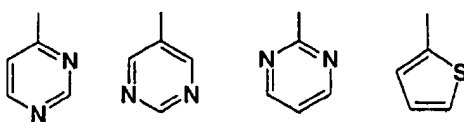
and A³ are the same as or different from each other and each represents phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group or morpholyl group which may optionally have substituents, respectively; (7) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each is a group represented by the formula:

10

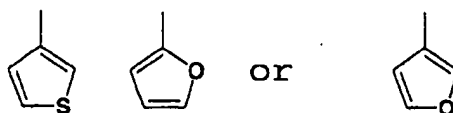


15

20

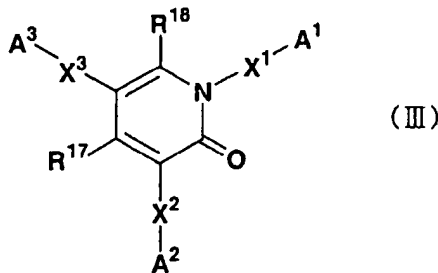


25



which may be substituted; (8) the compound according to the above (2), a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each is optionally substituted with hydroxyl group, a halogen atom, amino group or nitrile group; (9) the compound according to the above (7), a salt thereof or hydrates thereof, wherein the substituents of A¹, A² and A³ are the same as or different from each other and each is hydroxyl group, a halogen atom or, amino group, nitrile group or nitro group; (10) the compound according to the above (1) or (2), a salt thereof or hydrates thereof, wherein Q is oxygen; (11) the compound according to the above (1) or (2), a salt thereof, hydrates thereof, wherein X¹, X² and X³ are the same as or different from each other and each represents single bond, -CH₂-, -CH(OH)-, -CH₂-CH₂-, -CH=CH-, -C≡C-, -O- or -CO-; (12) the compound according to the above (2), a salt thereof or hydrates thereof, wherein X¹, X² and X³ are single bonds; (13) the compound according to the above (2), a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ are the same as or different from each other and each represents hydrogen atom, fluorine, chlorine, bromine, iodine, methyl group, ethyl group, n-propyl group or isopropyl group; (14) the compound according to the above (2), a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ represent hydrogen atom; (15) the compound according to the above (1) or (2), a salt thereof or hydrates thereof, which is represented by the formula:

45

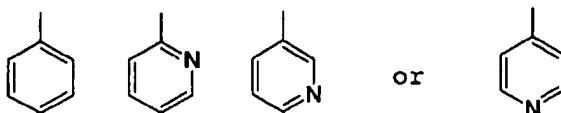


50

55

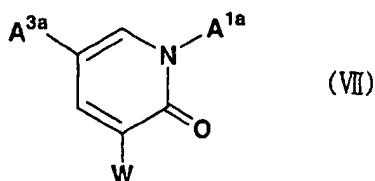
wherein X¹, X², X³, A¹, A², A³, R¹⁷ and R¹⁸ have the same meanings as defined in the above (2); (16) the compound according to the above (15), a salt thereof or hydrates thereof, wherein A¹, A² and A³ are same as or different from each other and each represents optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or 5- to 14-membered aromatic

heteroring; (16) the compound according to the above (15), a salt thereof or hydrates thereof, wherein A¹, A² and A³ are same as or different from each other and each represents optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or 5- to 14-membered aromatic heteroring; (17) the compound according to the above (15), a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each represents optionally substituted phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group or morpholyl group; (18) the compound according to the above (15), a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each represents a group represented by the following formula:

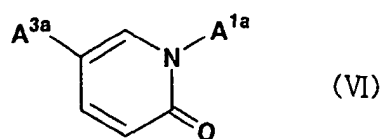


which may be substituted; (19) the compound according to the above (15), a salt thereof or hydrates thereof, wherein the bonding site of the substituent at A¹, A² and/or A³ are α -position of the carbon atom bonding to the group X¹, X² and X³, respectively; (20) the compound according to the above (15), a salt thereof or hydrates thereof, wherein X¹, X² and X³ are single bonds; (21) the compound according to the above (15), a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ are hydrogen atoms; (22) the compound according to the above (1), a salt thereof or hydrates thereof, which is any one of compounds selected from: 3-(2-cyanophenyl)-5-(2-methylsulfonylaminophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-dimethylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-[3-(5-methoxymethyl-2-oxazolidinon-3-yl)-phenyl]-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminocarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyano-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetylaminomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetoxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-diethylaminomethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-hydroxymethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-benzyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-phenyl-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1,5-diphenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-methoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(thiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-fluorophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(thiophen-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3-furfuryl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-furfuryl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-methoxycarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(4-methoxy-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-

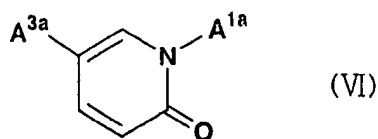
dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-chlorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-tolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-trifluoromethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(thiophen-3-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-furfuryl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-tolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-trifluoromethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-methoxypyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-benzoyloxymethylpyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-ethylthiopyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxypyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-chloropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-fluoropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(thiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2,6-dimethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one; 2-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(6-diethylaminomethyl-2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-hydroxypyridin-6-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-(2-aminobenzothiazol-6-yl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-benzyl-1,2,3,6-tetrahydropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-[2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(6-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(5-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3-hydroxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-phenyl-5-(2-thiazolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-methoxypyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one; 1-(4-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-(3-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-aminotoluen-4-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(dimethylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(piperidinoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(pyrrolidinoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(diisopropylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(4-piperidinobutyl-1-oxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(4-nitrophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-phenyl-5-(2-pyridyl)-3-(2-thiazolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-fluoropyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-cyanopyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-naphthyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-naphthyl)-1,2-dihydropyridin-2-one; 5-(2-aminopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 5-(2-bromopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-morpholinopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-hydroxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(4-piperidyl)oxy]phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-[3-(N-acetyl)piperidin-4-yl-oxy]phenyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-[1-(methanesulfonyl)piperidin-4-yl-oxy]phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-[3-(N-methylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(6-chloro-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-nitrotoluen-4-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)thiophen-3-yl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; and 3-(2-ethoxycarbonylvinylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; (23) a process for producing a compound represented by the formula:



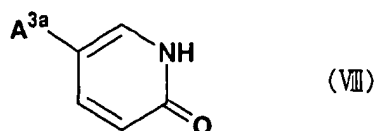
10 (wherein, each A^{1a} and A^{3a} has the same meaning as defined below; and W represents a halogen atom) or a salt thereof, which comprises subjecting the compound represented by the formula:



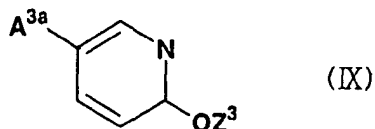
20 (wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group) or a salt thereof to a halogenation reaction; (24) a process for producing a compound represented by the formula:



35 (wherein A^{1a} and A^{3a} have the same meanings as defined above) or a salt thereof, which comprises subjecting the compound represented by the formula:

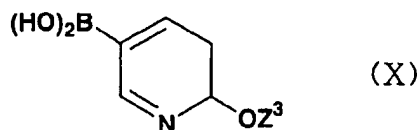


45 (wherein A^{3a} has the same meaning as defined above) or a salt thereof and a boronic acid derivative represented by the formula A^{1a}B(OH)₂ (wherein A^{1a} represents an optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or 5- to 14-membered aromatic heteroring) to a coupling reaction in the presence of a copper compound; (25) the production process according to the above (24), which comprises subjecting the compound represented by the above formula (VIII) or a salt thereof produced by subjecting the compound represented by the formula:

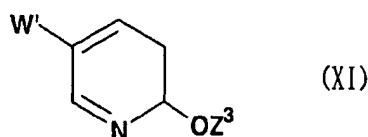


(wherein A^{3a} has the same meaning as defined above; and Z³ indicates a protecting group of an alcoholic hydroxy

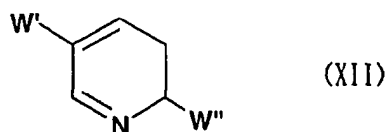
group) to de-protecting reaction and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (26) the production process according to the above (24), which comprises producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound represented by the above formula (IX) or a salt thereof produced by subjecting a boronic acid derivative represented by the formula:



15 (wherein Z^3 has the same meaning as defined above) or a salt thereof and the compound represented by the formula $A^{3a}.Z^1$ (wherein A^{3a} has the same meaning as defined above; and Z^1 represents a halogen atom) or a salt thereof to a coupling reaction in the presence of a palladium catalyst, to a de-protecting reaction; and then subjecting the compound (VIII) or a salt thereof and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (27) the production process according to the above (24), which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the formula:

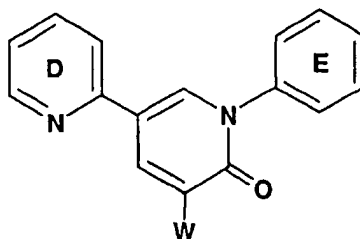


30 (wherein Z^3 has the same meaning as defined above; and W' represents a halogen atom) or a salt thereof and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX) or a salt thereof by subjecting the compound (X) or a salt and the compound represented by the formula $A^{3a}.Z^1$ (wherein A^{3a} and Z^1 have the same meanings as defined above) or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX) or a salt thereof to a de-protecting reaction; and then subjecting the compound (VIII) and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (28) the production process according to the above (24), which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the above formula (XI) or a salt thereof produced by reacting the compound represented by the formula:



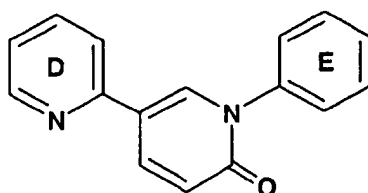
50 (wherein W' and W'' are the same as or different from each other and each represents halogen atoms) or a salt thereof and the compound represented by the formula Z^3OM (wherein Z^3 has the same meaning as defined above; and M represents an alkali metal atom) and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX) or a salt thereof by subjecting the compound (X) or a salt thereof and the compound represented by the formula $A^{3a}.Z^1$ (wherein A^{3a} and Z^1 have the same meanings as defined above) or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX) or a salt thereof to a de-protecting reaction; and then subjecting the compound (VIII) and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (29) the production process according to the above (23), which comprises subjecting the compound represented by the above formula (VI) and

produced by the production process according to any of the above (24) to (28) or a salt thereof to a halogenation reaction; (30) the production process according to the above (23) or (29), wherein W is bromine or iodine; (31) the production process according to the above (23) or (29), wherein the halogenation reaction for producing the compound (VII) or a salt thereof is (1) a bromination reaction using N-bromosuccinimide or acetic acid-bromine or (2) an iodination reaction using N-iodosuccinimide or iodine; (32) the production process according to the above (23) or (29), wherein the halogenation reaction for producing the compound (VII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent; (33) the production process according to the above (23) or (29), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (34) the production process according to any of the above (24) to (28), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (35) the production process according to any of the above (24) to (29), wherein the copper compound used for a coupling reaction using the compound (VIII) or a salt thereof is copper acetate or di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride; (36) the production process according to any of the above (24) to (29), wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out in the presence of a base; (37) the production process according to the above (36), wherein the base is triethylamine, pyridine or tetramethylethylenediamine; (38) the production process according to any of the above (24) to (29), wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent; (39) the production process according to any of the above (25) to (29), wherein Z³ is a C₁₋₆ alkyl group or a C₁₋₆ aralkyl group; (40) the production process according to the above (25) to (29), wherein the reaction of de-protection of the compound (IX) or a salt thereof is carried out in the presence of an acid; (41) the production process according to the above (40), wherein the acid is hydrochloric acid; (42) the production process according to the above (26) to (29), wherein a catalyst in the coupling reaction using the compound (X) or a salt thereof is palladium acetate and triphenylphosphine; (43) the production process according to the above (26) to (29), wherein the coupling reaction using the compound (X) or a salt thereof is carried out in the presence of a base; (44) the production process according to the above (43), wherein the base is cesium carbonate, sodium carbonate or potassium carbonate; (45) the production process according to any of the above (27) to (29), wherein W' is bromine; (46) the production process according to the above (27) to (29), wherein the base used for the reaction of the compound (XI) or a salt thereof with trimethoxyborane is n-butyllithium; (47) the production process according to the above (28) or (29), wherein W' and W'' are bromine; (48) the production process according to the above (28) or (29), wherein the compound represented by the formula Z³OM is sodium methoxide or sodium ethoxide; (49) a process for producing a compound represented by the formula:



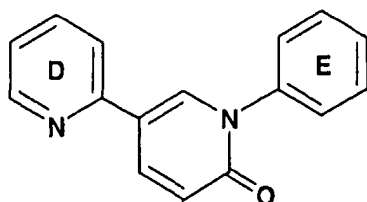
(VII)

(wherein, the ring D and the ring E have the same meanings as defined below; and W has the same meaning as defined above) or a salt thereof, which comprises subjecting a compound represented by the formula:



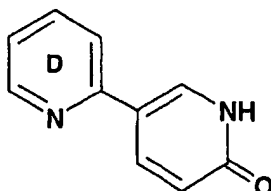
(VI)'

(wherein, the ring D ring indicates an optionally substituted pyridine ring; and the ring E represents an optionally substituted benzene ring) or a salt thereof to a halogenation reaction; (50) a process for producing a compound represented by the formula:



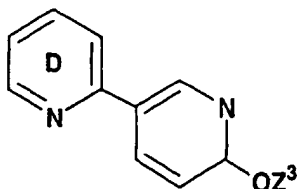
(VI)'

(wherein, the ring D and the ring E have the same meanings as defined above) or a salt thereof, which comprises subjecting the compound represented by the formula:



(VIII)'

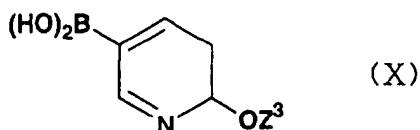
(wherein the ring D has the same meaning as defined above) or a salt thereof and a boronic acid derivative represented by the formula PhB(OH)_2 (wherein Ph indicates an optionally substituted phenyl group) to a coupling reaction in the presence of a copper compound; (51) the production process according to the above (50), which comprises subjecting the compound represented by the above formula (VIII)' or a salt thereof produced by subjecting the compound represented by the formula:



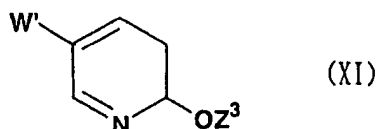
(IX)'

(wherein the ring B and Z^3 have the same meanings as defined above) or a salt thereof to a de-protecting reaction, and a boronic acid derivative represented by the formula PhB(OH)_2 (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (52) the production process according to the above (50), which comprises producing the compound represented by the above formula (VII)' or a salt thereof by subjecting the compound represented by the above formula (IX)' or a salt thereof produced by subjecting a boronic

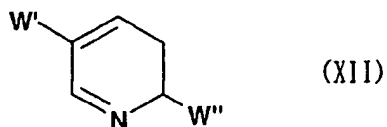
acid derivative represented by the formula:



10 (wherein Z^3 has the same meaning as defined above) or a salt thereof and an optionally substituted 2-halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst to a de-protecting reaction; and then
 15 subjecting the compound (VIII)' or a salt thereof and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound;
 (53) the production process according to the above (50), which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the formula:

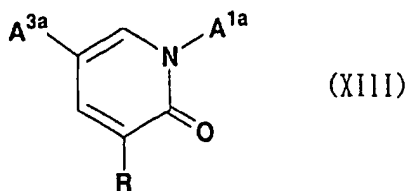


25 (wherein Z^3 has the same meaning as defined above; and W' represents a halogen atom) or a salt thereof and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX)' or a salt thereof
 by subjecting the compound (X) or a salt thereof and an optionally substituted 2-halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula
 30 (VIII) or a salt thereof by subjecting the compound (IX)' or a salt to a de-protecting reaction; and then subjecting the compound (VIII)' and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) in the presence of a copper compound; (54) the production process according to the above (50),
 which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the above formula (XI) or a salt thereof produced by reacting the compound represented
 35 by the formula:

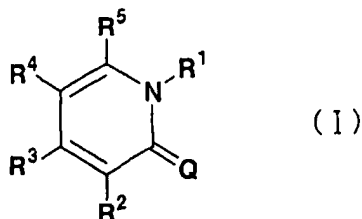


45 (wherein W' and W'' are the same as or different from each other and each represents halogen atoms) or a salt thereof and the compound represented by the formula $Z^3\text{OM}$ (wherein Z^3 and M have the same meanings as defined above),
 and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX)' or a salt thereof by subjecting the compound (X) or a salt and an optionally substituted 2-halogenopyridine or a salt thereof
 50 to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX)' or a salt to a de-protecting reaction; and then subjecting the compound (VIII)' and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound; (55) the production process according to the above (25), which comprises subjecting the compound represented by the above formula (VI)' and
 produced by the production process according to any of the above (29) to (32) or a salt thereof to a halogenation
 55 reaction; (56) the production process according to the above (49) or (55), wherein W is bromine or iodine; (57) the production process according to the above (49) or (55), wherein the halogenation reaction for producing the compound (VII) or a salt thereof is (1) a bromination reaction using N-bromosuccinimide or acetic acid-bromine, or (2) an iodination reaction using N-iodosuccinimide or iodine; (58) the production process according to the above (49) or (55), wherein

the halogenation reaction for producing the compound (VII) or a salt thereof is carried out using N, N-dimethylformamide as a solvent; (59) the production process according to the above (49) or (55), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (60) the production process according to any of the above (50) to (54), wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (61) the production process according to any of the above (50) to (55), wherein the copper compound used for the coupling reaction using the compound (VIII) or a salt thereof is copper acetate or di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride; (62) the production process according to any of the above (50) to (55), wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out in the presence of a base; (63) the production process according to the above (62), wherein the base is triethylamine, pyridine or tetramethylethylenediamine; (64) the production process according to any of the above (50) to (55), wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent; (65) the production process according to any of the above (51) to (55), wherein Z³ is a C₁₋₆ alkyl group or an aralkyl group; (66) the production process according to the above (51) to (55), wherein the de-protection reaction of the compound (IX) or a salt thereof is carried out in the presence of an acid; (67) the production process according to the above (66), wherein the acid is hydrochloric acid; (68) the production process according to the above (52) to (55), wherein a catalyst in the coupling reaction using the compound (X) or a salt thereof is palladium acetate and triphenylphosphine; (69) the production process according to the above (52) to (55), wherein the coupling reaction using the compound (X) or a salt thereof is carried out in the presence of a base; (70) the production process according to the above (69), wherein the base is cesium carbonate, sodium carbonate or potassium carbonate; (71) the production process according to any of the above (53) to (55), wherein W' is bromine; (72) the production process according to the above (53) to (55), wherein the base used for the reaction of the compound (XI) or a salt thereof with trimethoxyborane is n-butyllithium; (73) the production process according to the above (54) or (55), wherein W' and W'' are bromine; (74) the production process according to the above (54) or (55), wherein the compound represented by the formula Z³OM is sodium methoxide or sodium ethoxide; (75) the production process according to any of the above (52) to (55), wherein the optionally substituted 2-halogenopyridine is an optionally substituted 2-bromopyridine; (76) a compound represented by the following formula or a salt thereof:



wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group; and R indicates hydrogen atom or a halogen atom; (77) the compound according to the above (76) or a salt thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group; (78) the compound according to the above (76) or a salt thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents an optionally substituted phenyl group, pyridyl group, pyrimidinyl group, thienyl group or furyl group; (79) the compound according to the above (76) or a salt thereof, wherein R is hydrogen atom or bromine; (80) a pharmaceutical composition comprising a compound represented by the following formula, a salt thereof or hydrates thereof:



in the formula, Q indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or the formula -X-A (wherein X indicates a single bond, a C₁₋₆ alkylene group which may optionally have a substituent, a C₂₋₆ alkenylene group which may optionally have a substituent, a C₂₋₆ alkynylene group which may optionally have a substituent, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicates hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q are independent of each other and each indicates an integer of 0, 1 or 2); and A indicates an optionally substituted C₃₋₈ cycloalkyl group, C₃₋₈ cycloalkenyl group, 5- to 14-membered non-aromatic heterocyclic group, C₆₋₁₄ aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group), provided that 3 groups among R¹, R², R³, R⁴ and R⁵ are always the same as or different from each other and each indicates -X-A; and the residual 2 groups always indicate hydrogen atom, a halogen atom or a C₁₋₆ alkyl group; (81) the pharmaceutical composition according to the above (80), wherein it is an inhibitor to an α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (hereinafter, referred to as "AMPA") receptor and/or a kainate receptor; (82) the pharmaceutical composition according to the above (80), wherein it is an inhibitor to an AMPA receptor; (83) the pharmaceutical composition according to the above (80), wherein it is an inhibitor to a kainate receptor; (84) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for the diseases in which an AMPA receptor or a kainate receptor is participated; (85) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for the diseases in which a kainate receptor is participated; (86) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for acute neurodegenerative disease; (87) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for cerebrovascular disorders at acute stage, head injury, spinal cord injury, neuropathies due to hypoxia or hypoglycemia; (88) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for chronic neurodegenerative disease; (89) the pharmaceutical composition according to the above (80), which is a therapeutic or preventive agent for Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis or spinocerebellar degeneration; (90) the pharmaceutical composition according to the above (80), which is an agent for treating or preventing epilepsy, hepatic encephalopathy, peripheral neuropathy, Parkinson's syndrome, spasticity, pain, neuralgia, schizophrenia, anxiety, drug abuse, nausea, emesis, dysuria, paropsia caused by glaucoma, paracusis caused by antibiotics or food poisoning; (91) the pharmaceutical composition according to the above (80), which is an agent for treating or preventing infectious encephalomyelitis, cerebrovascular senile dementia or dementia or neurosis caused by cerebrospinal meningitis; (92) the pharmaceutical composition according to the above (91), wherein the infectious encephalomyelitis is HIV encephalomyelitis; (93) the pharmaceutical composition according to the above (80), which is an agent for treating or preventing demyelinating disease; (94) the pharmaceutical composition according to the above (93), wherein the demyelinating disease is encephalitis, acute disseminated encephalomyelitis, multiple sclerosis, acute polyradiculoneuritis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, Marchifava-Bignami disease, central pontine myelinolysis, neuromyelitis optica, Devic disease, Balo disease, HIV myelopathy, HTLV myelopathy, progressive multifocal leukoencephalopathy or secondary demyelinating disease; (95) the pharmaceutical composition according to the above (94), wherein the secondary demyelinating disease is CNS erythematodes, polyarteritis nodosa, Sjogren's syndrome, sarcoidosis or isolated cerebral vasculitis; and the like.

[0010] The present invention provides a process for preventing or treating diseases in which AMPA receptor or kainate receptor is participated, by dosing a pharmacologically effective dose of the compound represented by the formula (I), a salt thereof or hydrates thereof to a patient.

[0011] The present invention provides use of the compound represented by the formula (I), a salt thereof or hydrates thereof for producing a therapeutic or preventive agent for diseases in which AMPA receptor or kainate receptor is participated.

[0012] In the present invention, "the diseases in which AMPA receptor or kainate receptor is participated" include acute neurodegenerative disease; cerebrovascular disorders at acute stage; head injury; spinal cord injury; and neu-

ropathies due to hypoxia or hypoglycemia; chronic neurodegenerative disease; Alzheimer's disease; Parkinson's disease; Huntington's chorea; amyotrophic lateral sclerosis; spinocerebellar degeneration; epilepsy; hepatic encephalopathy; peripheral neuropathy; Parkinson's syndrome; spasticity; pain; neuralgia; schizophrenia; anxiety; drug abuse; nausea; emesis; dysuria; paropsia caused by glaucoma; paraculis caused by antibiotics; food poisoning; ; infectious encephalomyelitis; cerebrovascular dementia; dementia or neurosis caused by meningitis; and demyelinating diseases.

Detailed Description of the Invention

[0013] As hereunder, meanings of the symbols, terms, etc. mentioned in the specification of this application will be explained, whereby the present invention will be illustrated in detail.

[0014] As "acute neurodegenerative disease" in the present invention, for example, cerebrovascular disorders at acute stage (subarachnoid hemorrhage, cerebral infarction and the like), head injury, spinal cord injury, and neuropathies due to hypoxia or hypoglycemia; and the like are mentioned. As "chronic neurodegenerative disease", for example, Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis, spinocerebellar degeneration and the like are mentioned. As "infectious encephalomyelitis", for example, HIV encephalomyelitis is mentioned, and as "demyelinating disease", for example, encephalitis, acute disseminated encephalomyelitis, multiple sclerosis, acute polyradiculoneuritis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, Marchifava-Bignami disease, central pontine myelinolysis, neuromyelitis optica, Devic disease, Balo disease, HIV myelopathy, HTLV myelopathy, progressive multifocal leukoencephalopathy, secondary demyelinating disease and the like are mentioned. As "the secondary demyelinating disease" mentioned above, for example, CNS lupus erythematoses, polyarteritis nodosa, Sjogren's syndrome, sarcoidosis, isolated cerebral vasculitis and the like are mentioned.

[0015] The term "and/or" used in the present invention is used in the meaning that both cases in case of "and" and in case of "or" are included.

[0016] Incidentally, in the specification of this application, although structural formula of a compound may express a certain isomer for the sake of convenience, the present invention covers all isomers such as geometrical isomers resulted from the structure of the compound, optical isomers due to asymmetric carbon, rotamers, stereo isomers and tautomers as well as a mixture of isomers and the present invention is not limited to the description of the formula given for the sake of convenience but may be another isomer or may be a mixture. Accordingly, although it is possible that an asymmetric carbon atom is present in a molecule and accordingly that optically active substance and racemic substance may be present, the present invention is not limited thereto but covers any of them. Further, crystal polymorphism may be present but, again, there is no limitation but any of single crystal form or a mixture will do. The compound (I) or its salt related to the present invention may be an anhydride or a hydrate, and either of them are included in the scope of claim for patent in the present invention. The metabolite which is generated by decomposing the compound (I) related to the present invention *in vivo*, and the prodrug of the compound (I) or its salt related to the present invention produce are also included in the scope of claim for patent in the present invention.

[0017] The "halogen atom" used in the present invention indicates fluorine, chlorine, bromine, iodine and the like, and the preferable atom include fluorine, chlorine and bromine.

[0018] The "C₁₋₆ alkyl group" used in the present invention indicates an alkyl group having 1 to 6 carbons, and examples include linear chain or branched chain alkyl groups such as methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, iso-butyl group, sec-butyl group, tert-butyl group, n-pentyl group, 1,1-dimethylpropyl group, 1,2-dimethylpropyl group, 2,2-dimethylpropyl group, 1-ethylpropyl group, 2-ethylpropyl group, n-hexyl group, 1-methyl-2-ethylpropyl group, 1-ethyl-2-methylpropyl group, 1,1,2-trimethylpropyl group, 1-propylpropyl group, 1-methylbutyl group, 2-methylbutyl group, 1,1-dimethylbutyl group, 1,2-dimethylbutyl group, 2,2-dimethylbutyl group, 1,3-dimethylbutyl group, 2,3-dimethylbutyl group, 2-ethylbutyl group, 2-methylpentyl group, 3-methylpentyl group, and the like.

[0019] The "C₂₋₆ alkenyl group" used in the present invention indicates an alkenyl group having 2 to 6 carbons, and examples of the preferable group include vinyl group, allyl group, 1-propenyl group, 2-propenyl group, iso-propenyl group, 2-methyl-1-propenyl group, 3-methyl-1-propenyl group, 2-methyl-2-propenyl group, 3-methyl-2-propenyl group, 1-butenyl group, 2-butenyl group, 3-butenyl group, 1-pentenyl group, 1-hexenyl group, 1,3-hexadienyl group, 1,6-hexadienyl group, and the like.

[0020] The "C₂₋₆ alkynyl group" used in the present invention indicates an alkynyl group having 2 to 6 carbons, and examples of the preferable group include ethynyl group, 1-propynyl group, 2-propynyl group, 1-butylnyl group, 2-butylnyl group, 3-butylnyl group, 3-methyl-1-propynyl group, 1-ethynyl-2-propynyl group, 2-methyl-3-propynyl group, 1-pentylnyl group, 1-hexynyl group, 1,3-hexadiynyl group, 1,6-hexadiynyl group, and the like.

[0021] The "C₁₋₆ alkoxy group" used in the present invention indicates an alkoxy group having 1 to 6 carbons, and examples include methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentyloxy group, iso-pentyloxy group, sec-pentyloxy group, n-hexoxy group, iso-hexoxy group, 1,1-dimethylpropoxy group, 1,2-dimethylpropoxy group, 2,2-dimethylpro-

poxo group, 2-ethylpropoxo group, 1-methyl-2-ethylpropoxo group, 1-ethyl-2-methylpropoxo group, 1,1,2-trimethylpropoxo group, 1,1,2-trimethylpropoxo group, 1,1-dimethylbutoxy group, 1,2-dimethylbutoxy group, 2,2-dimethylbutoxy group, 2,3-dimethylbutoxy group, 1,3-dimethylbutoxy group, 2-ethylbutoxy group, 1,3-dimethylbutoxy group, 2-methylpentoxo group, 3-methylpentoxo group, hexyloxy group, and the like.

5 [0022] The " C_{2-6} alkenyloxy group" used in the present invention indicates an alkenyloxy group having 2 to 6 carbons, and examples of the preferable group include vinyloxy group, allyloxy group, 1-propenyloxy group, 2-propenyloxy group, iso-propenyloxy group, 2-methyl-1-propenyloxy group, 3-methyl-1-propenyloxy group, 2-methyl-2-propenyloxy group, 3-methyl-2-propenyloxy group, 1-butenyloxy group, 2-butenyloxy group, 3-butenyloxy group, 1-pentenyl group, 1-hexenyloxy group, 1,3-hexadienyloxy group, 1,6-hexadienyloxy group, and the like.

10 [0023] The " C_{3-8} cycloalkyl group" used in the present invention indicates a cycloalkyl group composed of 3 to 8 carbon atoms, and examples include cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, cyclooctyl group, and the like.

[0024] The " C_{3-8} cycloalkenyl group" used in the present invention indicates a C_{3-8} cycloalkenyl group composed of 3 to 8 carbon atoms, and examples include cyclopropen-1-yl, cyclopropen-3-yl, cyclobuten-1-yl, cyclobuten-3-yl, 1,3-cyclobutadien-1-yl, cyclopenten-1-yl, cyclopenten-3-yl, cyclopenten-4-yl, 1,3-cyclopentadien-1-yl, 1,3-cyclopentadien-2-yl, 1,3-cyclopentadien-5-yl, cyclohexen-1-yl, cyclohexen-3-yl, cyclohexen-4-yl, 1,3-cyclohexadien-1-yl, 1,3-cyclohexadien-2-yl, 1,3-cyclohexadien-5-yl, 1,4-cyclohexadien-3-yl, 1,4-cyclohexadien-1-yl, cyclohepten-1-yl, cyclohepten-3-yl, cyclohepten-4-yl, cyclohepten-5-yl, 1,3-cyclohepten-2-yl, 1,3-cyclohepten-1-yl, 1,3-cycloheptadien-5-yl, 1,3-cycloheptadien-6-yl, 1,4-cycloheptadien-3-yl, 1,4-cycloheptadien-2-yl, 1,4-cycloheptadien-1-yl, 1,4-cycloheptadien-6-yl, 1,3,5-cycloheptatrien-3-yl, 1,3,5-cycloheptatrien-2-yl, 1,3,5-cycloheptatrien-1-yl, 1,3,5-cycloheptatrien-7-yl, cycloocten-1-yl, cycloocten-3-yl, cycloocten-4-yl, cycloocten-5-yl, 1,3-cyclooctadien-2-yl, 1,3-cyclooctadien-1-yl, 1,3-cyclooctadien-5-yl, 1,3-cyclooctadien-6-yl, 1,4-cyclooctadien-3-yl, 1,4-cyclooctadien-2-yl, 1,4-cyclooctadien-1-yl, 1,4-cyclooctadien-6-yl, 1,4-cyclooctadien-7-yl, 1,5-cyclooctadien-3-yl, 1,5-cyclooctadien-2-yl, 1,3,5-cyclooctatrien-3-yl, 1,3,5-cyclooctatrien-2-yl, 1,3,5-cyclooctatrien-1-yl, 1,3,5-cyclooctatrien-7-yl, 1,3,6-cyclooctatrien-2-yl, 1,3,6-cyclooctatrien-1-yl, 1,3,6-cyclooctatrien-5-yl, 1,3,6-cyclooctatrien-6-yl group, and the like.

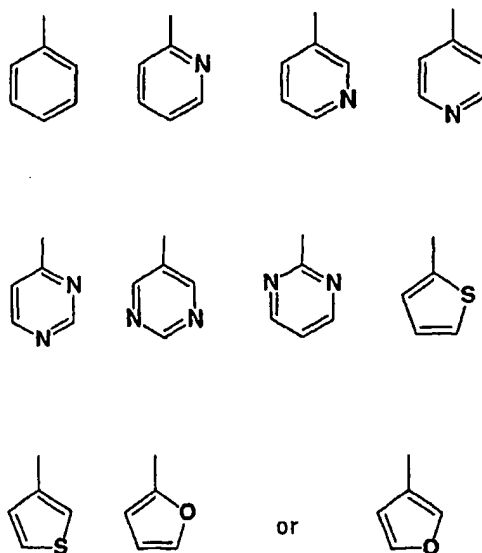
[0025] The "5 to 14 membered non-aromatic heterocyclic group" used in the present invention means a mono-cyclic type, di-cyclic type, or tri-cyclic type 5 to 14 membered non-aromatic heterocyclic group which contains one or more of hetero atoms selected from a group which consists of nitrogen atom, sulfur atom and oxygen atom. Specific examples in the group include, for example, pyrrolidinyl group, pyrrol group, piperidinyl group, piperazinyl group, imidazolyl group, pyrazolidyl group, imidazolidyl group, morpholyl group, tetrahydrofuryl group, tetrahydropyranyl group, pyrrolinyl group, dihydrofuryl group, dihydropyranyl group, imidazolyl group, oxazolyl group, and the like. Further, a group derived from a pyridone ring and a non-aromatic condensed ring (for example, a group derived from a phthalimide ring, a succinimide ring, and the like) are also included in the non-aromatic heterocyclic group.

[0026] The " C_{6-14} aromatic hydrocarbocyclic group" and the "aryl group" used in the present invention mean an aromatic hydrocarbocyclic group having which is composed of 6 to 14 carbon atoms, and a mono-cyclic group, and a condensed group of a di-cyclic group, a tri-cyclic group and the like are also included. Specific examples in the group include phenyl group, indenyl group, 1-naphthyl group, 2-naphthyl group, azulenyl group, heptalenyl group, biphenyl group, indathenyl group, acenaphthyl group, fluorenyl group, phenalenyl group, phenanthrenyl group, anthracenyl group, cyclopentacyclooctenyl group, benzocyclooctenyl group etc.

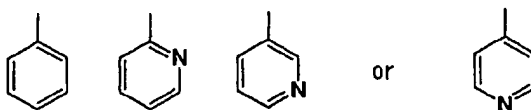
40 [0027] The "5 to 14 membered aromatic heterocyclic group" and the "heteroaryl group" used in the present invention mean a mono-cyclic type, di-cyclic type, or tri-cyclic type 5 to 14 membered aromatic heterocyclic group which contains one or more of hetero atoms selected from a group which consists of nitrogen atom, sulfur atom and oxygen atom. For example, specific examples in the group include 1) aromatic heterocyclic groups containing nitrogen such as pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, triazolyl group, tetrazolyl group, benzotriazolyl group, pyrazolyl group, imidazolyl group, benzimidazolyl group, indolyl group, iso-indolyl group, indoliziny group, prenyl group, indazolyl group, quinolyl group, iso-quinolyl group, quinoliziny group, phthalazyl group, naphthylidiny group, quinoxalyl group, quinazoliny group, cynnoliny group, pteridinyl group, imidazotriazinyl group, pyrazinopyridazinyl group, acridinyl group, phenanthridinyl group, carbazolyl group, carbazoliny group, perimidinyl group, phenanthrolinyl group, phenaciny group, imidazopyridinyl group, imidazopyrimidinyl group, pyrazolopyridinyl group, pyrazolopyrimidinyl group etc; 2) aromatic heterocyclic groups containing sulfur such as thienyl group or benzothienyl group; 3) aromatic heterocyclic groups containing oxygen such as furyl group, pyranyl group, cyclopentapyranyl group, benzofuryl group or iso-benzofuryl group; and 4) aromatic heterocyclic groups containing 2 or more of different hetero atoms such as thiazolyl group, iso-thiazolyl group, benzothiazolyl group, benzthiadiazolyl group, phenothiazinyl group, isoxazolyl group, furazanyl group, phenoxazinyl group, oxazolyl group, isoxazolyl group, benzoxazolyl group, oxadiazolyl group, pyrazoloxadiazolyl group, imidazothiazolyl group, thienofuranyl group, furopyrrolyl group or pyridoxadiny group.

[0028] The groups indicated by A, A¹, A² and A³ in the formula (I) in the present invention indicate independently an optionally substituted C_{3-8} cycloalkyl group, an optionally substituted C_{3-8} cycloalkenyl group, an optionally substituted

5 to 14 membered non-aromatic heterocyclic group, an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or an optionally substituted 5 to 14 membered aromatic heterocyclic group, and each of the groups has the same meanings as the above definitions, respectively. The preferable group in A, A¹, A² and A³ is not specifically limited, but the more preferable group includes phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group and morpholinyl group which may be substituted, respectively, etc. The more preferable group includes a group represented by the formula:



which may optionally have substituents respectively, etc., and the most preferable group includes a group represented by the formula:



which may optionally have substituents respectively, etc.

[0029] Examples of the preferable group in the "substituents" of the groups indicated by A, A¹, A² and A³ in the formula (I) include a group such as hydroxy group, a halogen atom, nitrile group, nitro group, a C₁₋₆ alkyl group, C₂₋₆ alkenyl group, C₂₋₆ alkynyl group, C₁₋₆ alkoxy group, C₂₋₆ alkenyloxy group, C₂₋₆ alkynyloxy group, C₁₋₆ alkylthio group, C₂₋₆ alkenylthio group, C₂₋₆ alkynylthio group, amino group, a substituted carbonyl group, C₁₋₆ alkylsulfonyl group, C₂₋₆ alkenylsulfonyl group, C₂₋₆ alkynylsulfonyl group, C₁₋₆ alkylsulfinyl group, C₂₋₆ alkenylsulfinyl group, C₂₋₆ alkynylsulfinyl group, formyl group, aralkyl group, heteroarylalkyl group, aralkyloxy group, heteroarylalkyloxy group, C₃₋₈ cycloalkyl group, C₃₋₈ cycloalkenyl group, 5 to 14 membered non-aromatic heterocyclic group, C₆₋₁₄ aromatic hydrocarbon group, 5 to 14 membered aromatic heterocyclic group etc., which may be substituted, respectively.

[0030] Examples of the preferable group in the "halogen atom" include fluorine atom, chlorine atom, bromine atom, iodine atom etc., and the more preferable example includes fluorine atom, chlorine atom and bromine atom.

[0031] Examples of the preferable group in the "C₁₋₆ alkyl group which may optionally have substituents" include methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, iso-butyl group, tert-butyl group, n-pentyl group, iso-pentyl group, neopentyl group, n-hexyl group, 1-methylpropyl group, 1,2-dimethylpropyl group, 2-ethylpropyl group, 1-methyl-2-ethylpropyl group, 1-ethyl-2-methylpropyl group, 1,1,2-trimethylpropyl group, 1-methylbutyl group,

2-methylbutyl group, 1,1-dimethylbutyl group, 2,2-dimethylbutyl group, 2-ethylbutyl group, 1,3-dimethylbutyl group, 2-methylpentyl group, 3-methylpentyl group etc. Examples of the preferable group in the "C₂₋₆ alkenyl group which may optionally have substituents" include a vinyl group, allyl group, 1-propenyl group, iso-propenyl group, 1-buten-1-yl group, 1-buten-2-yl group, 1-buten-3-yl group, 2-buten-1-yl group, 2-buten-2-yl group etc., which may be substituted, respectively. Examples of the preferable group in the "C₂₋₆ alkynyl group which may optionally have substituents respectively" include an ethynyl group, 1-propynyl group, 2-propynyl group, butynyl group, pentynyl group, hexynyl group etc., which may be substituted, respectively. Further, preferable examples of the "substituents" in the "which may optionally have substituents" include 1 or more groups selected from hydroxy group, nitrile group, a halogen atom, an N-C₁₋₆ alkylamino group, an N,N-di-C₁₋₆ alkylamino group, an N-C₂₋₆ alkenylamino group, an N,N-di-C₂₋₆ alkenylamino group, an N-C₂₋₆ alkynylamino group, an N,N-di-C₂₋₆ alkynylamino group, a C₆₋₁₄ aromatic hydrocarbocyclic group (for example, phenyl group etc.), a 5 to 14 membered aromatic heterocyclic group (for example, thienyl group, furyl group, pyridyl group, pyridazyl group, pyrimidinyl group, pyrazyl group etc.), an aralkyloxy group, a heteroaryloxy group, a TBDMS-oxy group, a C₁₋₆ alkylsulfonylamino group, a C₂₋₆ alkenylsulfonylamino group, a C₂₋₆ alkynylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group, a C₂₋₆ alkenylcarbonyloxy group, a C₂₋₆ alkynylcarbonyloxy group, a C₁₋₆ alkylcarbamoyl group, a C₂₋₆ alkenylcarbamoyl group, a C₂₋₆ alkynylcarbamoyl group, and the like.

[0032] Preferable examples in the "C₁₋₆ alkoxy group which may optionally have substituents" include methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentoxy group, iso-pentoxy group, sec-pentoxy group, tert-pentoxy group, n-hexoxy group, iso-hexoxy group, 1,2-dimethylpropoxy group, 2-ethylpropoxy group, 1-methyl-2-ethylpropoxy group, 1-ethyl-2-methylpropoxy group, 1,1,2-trimethylpropoxy group, 1,1-dimethylbutoxy group, 2,2-dimethylbutoxy group, 2-ethylbutoxy group, 1,3-dimethylbutoxy group, 2-methylpentoxy group, 3-methylpentoxy group, hexyloxy group etc. Preferable examples in the "C₂₋₆ alkenyloxy group which may optionally have substituents" include vinyloxy group, allyloxy group, 1-propenyloxy group, iso-propenyloxy group, 1-buten-1-yloxy group, 1-buten-2-yloxy group, 1-buten-3-yloxy group, 2-buten-1-yloxy group, 2-buten-2-yloxy group etc. Preferable examples in the "C₂₋₆ alkynyloxy group which may optionally have substituents" include ethynyloxy group, 1-propynyloxy group, 2-propynyloxy group, butynyloxy group, pentynyloxy group, hexynyloxy group etc. Further, preferable examples of the "substituents" in the "which may optionally have substituents" include 1 or more groups selected from an C₁₋₆ alkylamino group, an aralkyloxy group, hydroxy group, and the like.

[0033] Respectively preferable examples in the "C₁₋₆ alkylthio group which may optionally have substituents", "C₂₋₆ alkenylthio group which may optionally have substituents" and "C₂₋₆ alkynylthio group which may optionally have substituents" include a C₁₋₆ alkylthio group (for example, methylthio group, ethylthio group, n-propylthio group, iso-propylthio group, n-butylthio group, iso-butylthio group, tert-butylthio group, n-pentylthio group, iso-pentylthio group, neopentylthio group, n-hexylthio group etc.), a C₂₋₆ alkenylthio group (for example, vinylthio group, allylthio group, 1-propenylthio group, iso-propenylthio group, 1-buten-1-ylthio group, 1-buten-2-ylthio group, 1-buten-3-ylthio group, 2-buten-1-ylthio group, 2-buten-2-ylthio group etc.) and a C₂₋₆ alkynylthio group (for example, ethynylthio group, 1-propynylthio group, 2-propynylthio group, butynylthio group, pentynylthio group, hexynylthio group etc.), which may be optionally substituted by 1 or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group and nitro group.

[0034] Preferable examples in the "carbonyl group which was substituted" include a group which is represented by the formula -CO-W (examples of W in the formula include a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkoxy group, amino group, an N-C₁₋₆ alkylamino group, an N,N-di(C₁₋₆ alkyl)amino group, an N-C₂₋₆ alkenylamino group, an N,N-di(C₂₋₆ alkenyl) amino group, an N-C₂₋₆ alkynylamino group, an N,N-di(C₂₋₆ alkynyl)amino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group, an N-C₂₋₆ alkenyl-N-C₂₋₆ alkylamino group etc.).

[0035] Examples of the "substituents" in the "amino group which may optionally have substituents" include 1 or 2 groups selected from a C₁₋₆ alkyl group, C₂₋₆ alkenyl group, C₂₋₆ alkynyl group, C₁₋₆ alkylsulfonyl group, C₂₋₆ alkenylsulfonyl group, C₂₋₆ alkynylsulfonyl group, C₁₋₆ alkylcarbonyl group, C₂₋₆ alkenylcarbonyl group, C₂₋₆ alkynylcarbonyl group etc., which may be substituted, respectively. Preferable examples in the "substituents" of the C₁₋₆ alkyl group, C₂₋₆ alkenyl group, C₂₋₆ alkynyl group, C₁₋₆ alkylsulfonyl group, C₂₋₆ alkenylsulfonyl group, C₂₋₆ alkynylsulfonyl group, C₁₋₆ alkylcarbonyl group, C₂₋₆ alkenylcarbonyl group and C₂₋₆ alkynylcarbonyl group include hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkoxy group, a C₁₋₆ alkylthio group etc. Specifically preferable examples in the "amino group which may optionally have substituents" in particular include methylamino group, ethylamino group, n-propylamino group, iso-propylamino group, n-butylamino group, iso-butylamino group, tert-butylamino group, n-pentylamino group, iso-pentylamino group, neopentylamino group, n-hexylamino group, 1-methylpropylamino group, 1,2-dimethylpropylamino group, 2-ethylpropylamino group, 1-methyl-2-ethylpropylamino group, 1-ethyl-2-methylpropylamino group, 1,1,2-trimethylpropylamino group, 1-methylbutylamino group, 2-methylbutylamino group, 1,1-dimethylbutylamino group, 2,2-dimethylbutylamino group, 2-ethylbutylamino group, 1,3-dimethylbutylamino group, 2-methylpentylamino group, 3-methylpentylamino group, N,N-dimethylamino group, N,N-diethylamino group, N,N-di(n-propyl)amino group,

N,N-di(iso-propyl)amino group, N,N-di(n-butyl)amino group, N,N-di(iso-butyl)amino group, N,N-di(tert-butyl)amino group, N,N-di(n-pentyl)amino group, N,N-di(iso-pentyl)amino group, N,N-di(neopentyl)amino group, N,N-di(n-hexyl) amino group, N,N-di(1-methylpropyl)amino group, N,N-di(1,2-dimethylpropyl)amino group, N-methyl-N-ethylamino group, N-ethyl-N-(n-propyl)amino group, N-ethyl-N-(iso-propyl)amino group, vinylamino group, allylamino group, (1-propenyl)amino group, iso-propenylamino group, (1-buten-1-yl)amino group, (1-buten-2-yl)amino group, (1-buten-3-yl)amino group, (2-buten-1-yl)amino group, (2-buten-2-yl)amino group, N,N-divinylamino group, N,N-diallylamino group, N,N-di(1-propenyl)amino group, N,N-di(iso-propenyl)amino group, N-vinyl-N-allylamino group, ethynylamino group, 1-propynylamino group, 2-propynylamino group, butynylamino group, pentynylamino group, hexynylamino group, N,N-diethynylamino group, N,N-di(1-propynyl)amino group, N,N-di(2-propynyl)amino group, N,N-dibutynylamino group, N,N-dipentynylamino group, N,N-dihexynylamino group, hydroxymethylamino group, 1-hydroxyethylamino group, 2-hydroxyethylamino group, 3-hydroxy-n-propylamino group, methylsulfonylamino group, ethylsulfonylamino group, n-propylsulfonylamino group, iso-propylsulfonylamino group, n-butylsulfonylamino group, tert-butylsulfonylamino group, vinylsulfonylamino group, allylsulfonylamino group, iso-propenylsulfonylamino group, iso-pentenylsulfonylamino group, ethynylsulfonylamino group, methylcarbonylamino group, ethylcarbonylamino group, n-propylcarbonylamino group, iso-propylcarbonylamino group, n-butylcarbonylamino group, tert-butylcarbonylamino group, vinylcarbonylamino group, allylcarbonylamino group, iso-propenylcarbonylamino group, iso-pentenylcarbonylamino group, ethynylcarbonylamino group etc.

[0036] Respectively preferable examples in the "C₁₋₆ alkylsulfonyl group which may optionally have substituents", "C₂₋₆ alkenylsulfonyl group which may optionally have substituents", "C₂₋₆ alkynylsulfonyl group which may optionally have substituents", "C₁₋₆ alkylsulfinyl group which may optionally have substituents", "C₂₋₆ alkenylsulfinyl group which may optionally have substituents" and "C₂₋₆ alkynylsulfinyl group which may optionally have substituents" include methylsulfonyl group, ethylsulfonyl group, n-propylsulfonyl group, iso-propylsulfonyl group, n-butylsulfonyl group, tert-butylsulfonyl group, vinylsulfonyl group, allylsulfonyl group, iso-propenylsulfonyl group, iso-pentenylsulfonyl group, ethynylsulfonyl group, methylsulfinyl group, ethylsulfinyl group, n-propylsulfinyl group, iso-propylsulfinyl group, n-butylsulfinyl group, tert-butylsulfinyl group, vinylsulfinyl group, allylsulfinyl group, iso-propenylsulfinyl group, iso-pentenylsulfinyl group, ethynylsulfinyl group etc.

[0037] Preferable examples in the "aralkyl group" and "heteroarylalkyl group" include benzyl group, phenethyl group, naphthylmethyl group, naphthylethyl group, pyridylmethyl group, pyridylethyl group, thienylmethyl group, thienylethyl group etc., preferable examples in the "aralkyloxy group" include benzyloxy group, phenethyloxy group, phenylpropoxy group, naphthylmethyloxy group, naphthylethyloxy group, naphthylpropyloxy group etc., and preferable examples in the "heteroarylalkyloxy group" include pyridylmethyloxy group, pyrazinylmethyloxy group, pyrimidinylmethyloxy group, pyrrolylmethyloxy group, imidazolylmethyloxy group, pyrazolylmethyloxy group, quinolylmethyloxy group, iso-quinolylmethyloxy group, fulfuryloxy group, thienylmethyloxy group, thiazolylmethyloxy group etc.

[0038] Preferable examples in the "C₃₋₈ cycloalkyl group which may optionally have substituents" and "C₃₋₈ cycloalkenyl group which may optionally have a substituent" include a C₃₋₈ cycloalkyl group (for example, cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, and the like) and a C₃₋₈ cycloalkenyl group (for example, cyclopropenyl group, cyclopropenyl group, cyclobutenyl group, cyclopentenyl group, cyclohexenyl group, cycloheptenyl group, and the like) which may be optionally substituted respectively by 1 or more groups selected from hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group (for example, methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, iso-butyl group, tert-butyl group, n-pentyl group, iso-pentyl group, neopentyl group, n-hexyl group etc.), a C₁₋₆ alkoxy group (for example, methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentoxy group, iso-pentoxy group, sec-pentoxy group, tert-pentoxy group, n-hexoxy group etc.), a C₁₋₆ alkoxy C₁₋₆ alkyl group, an aralkyl group (for example, benzyl group, phenethyl group, naphthylmethyl group, naphthylethyl group etc.), and the like.

[0039] Preferable examples of the "5 to 14 membered non-aromatic heterocyclic group", "C₆₋₁₄ aromatic hydrocarbocyclic group" and "5 to 14 membered aromatic heterocyclic group" in "an optionally substituted 5 to 14 membered non-aromatic heterocyclic group", "an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group" and "an optionally substituted 5 to 14 membered aromatic heterocyclic group" are not specifically limited, but the more preferable "5 to 14 membered non-aromatic heterocyclic group" includes pyrrolidinyl group, pyrrolinyl group, piperidinyl group, piperazinyl group, imidazolyl group, pyrazolyl group, imidazolidinyl group, morpholinyl group, phthalimidoyl group, a succinimidoyl group etc.; the more preferable "C₆₋₁₄ aromatic hydrocarbocyclic group" includes phenyl group, indenyl group, naphthyl group, azulenyl group, heptalenyl group, biphenyl group etc.; the more preferable "5 to 14 membered aromatic heterocyclic group" includes pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, pyrazolyl group, imidazolyl group, thienyl group, furyl group, thiazolyl group, iso-thiazolyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, carbazolyl group, dioxinyl group etc., respectively. Further, preferable examples of the "substituents" in the "which may optionally have substituents" include 1 or more groups selected from hydroxy group, a halogen atom (for example, fluorine atom, chlorine atom, bromine atom, iodine atom etc.), nitrile group, a C₁₋₆ alkyl group (for example, methyl group, ethyl group,

n-propyl group, iso-propyl group, n-butyl group, iso-butyl group, tert-butyl group, n-pentyl group, iso-pentyl group, neopentyl group, n-hexyl group etc.), a C₁₋₆ alkoxy group (methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, sec-propoxy group, n-butoxy group, iso-butoxy group, sec-butoxy group, tert-butoxy group, n-pentoxy group, iso-pentoxy group, sec-pentoxy group, tert-pentoxy group, n-hexoxy group etc.), a C₁₋₆ alkoxy C₁₋₆ alkyl group (for example, methoxymethyl group, methoxyethyl group, ethoxymethyl group, ethoxyethyl group etc.), an aralkyl group (for example, benzyl group, phenethyl group, naphthylmethyl group, naphthylethyl group etc.), and the like. Further, an amino group, a cyclic amino group, and an alkoxyamino group which may optionally have substituents are also preferable as the substituents.

[0040] Q indicates NH, O or S in the formula (I), and is preferably O.

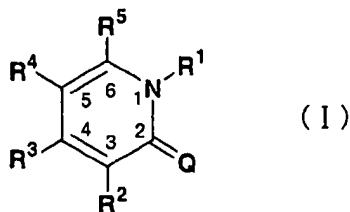
[0041] The groups indicated by X, X¹, X² and X³ in the present invention indicate the same or different single bonding, an optionally substituted C₁₋₆ alkylene group, an optionally substituted C₂₋₆ alkenylene group, an optionally substituted C₂₋₆ alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicate hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q indicates an integer of 0, 1 or 2 independently).

[0042] Specifically preferable examples in the above "C₁₋₆ alkylene group" is an alkylene group having 1 to 3 carbons, and examples include -CH₂-, -(CH₂)₂-, -CH(CH₃)-, -(CH₂)₃-, -CH(CH₃)-CH₂-, -CH₂-CH(CH₃)- etc. Specifically preferable examples in the above "C₂₋₆ alkenylene group" is an alkenylene group having 2 or 3 carbons, and examples include -CH=CH-, -CH=CH-CH₂-, -CH₂-CH=CH-, -C(CH₃)=CH-, -CH=C(CH₃)- etc. Specifically preferable examples in the above "C₂₋₆ alkynylene group" is an alkynylene group having 2 or 3 carbons, and examples include -C≡C-, -C≡C-CH₂-, -CH₂-C≡C- etc. Preferable examples in the substituents indicated by X, X¹, X² and X³ in the "C₁₋₆ alkylene group which may optionally have substituents", "C₂₋₆ alkenylene group which may optionally have substituents" or "C₂₋₆ alkynylene group which may optionally have substituents" include a halogen atom (for example, fluorine atom, chlorine atom, bromine atom, iodine atom etc.), hydroxy group, nitrile group, nitro group etc.

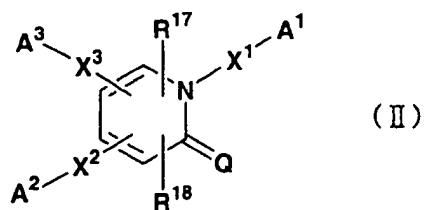
[0043] The preferable C₁₋₆ alkyl group represented by the R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ includes methyl group, ethyl group, n-propyl group, iso-propyl group, n-butyl group, tert-butyl group etc., and the preferable C₂₋₆ alkoxy group includes methoxy group, ethoxy group, n-propoxy group, iso-propoxy group, n-butoxy group, tert-butoxy group etc.

[0044] The preferable group in X, X¹, X² and X³ in the above formula (I) includes single bond, -CH₂-, -CH(OH)-, -CH(CN)-, -CH₂-CH₂-, -CH(OH)-CH₂-, -CH(CN)-CH₂-, -CH₂-CH(OH)-, -CH₂-CH(CN)-, -CH=CH-, -CH=CH-CH₂-, -CH=CH-CH(OH)-, -CH=CH-CH(CN)-, -CH(OH)-CH=CH-, -CH(CN)-CH=CH-, -C≡C-, -O-, -S-, -SO-, -SO₂-, -CO-, -NH-CO-NH-, -NH-CS-NH-, and the like; the more preferable group includes single bond, -CH₂-, -CH(OH)-, -CH(CN)-, -CH₂-CH₂-, -CH(OH)-CH₂-, -CH(CN)-CH₂-, -CH₂-CH(OH)-, -CH₂-CH(CN)-, -CH=CH-, -C≡C-, -CO-, and the like; the further preferable group are -CH₂-, -CH(OH)-, -CO-, and a single bond is most preferable.

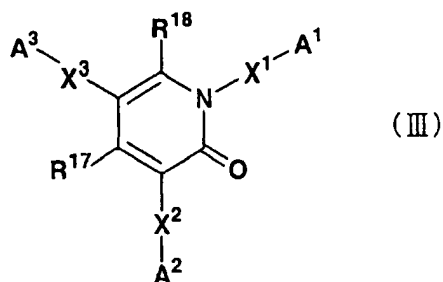
[0045] The preferable mode of in the compound according to the present invention represented by the formula:



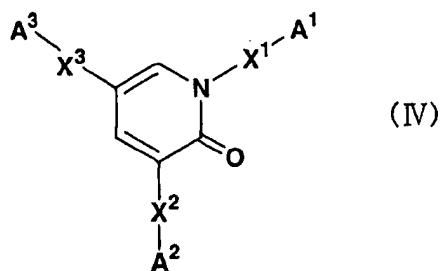
(wherein Q, R¹, R², R³, R⁴ and R⁵ have the same meanings as defined above), a salt thereof or hydrates thereof is not specifically limited. Among them, the preferable mode includes the compound, a salt thereof or hydrates thereof, wherein R¹ (namely, 1-position of a pyridone ring) is a group represented by the formula -X-A (X and A have the same meanings as defined above), two of the residual R², R³, R⁴ and R⁵ are a group represented by the formula -X-A (X and A have the same meanings as defined above), and the other two are hydrogen atom, a halogen atom or a C₁₋₆ alkyl group; namely, the compound represented by the formula:



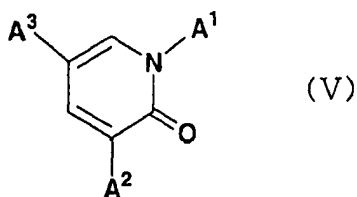
(wherein Q, X¹, X², X³, A¹, A², A³, R¹⁷ and R¹⁸ have the same meanings as defined above), a salt thereof or hydrates thereof. The more preferable mode includes the compound, a salt thereof or hydrates thereof, wherein Q is oxygen in the above formula (II); namely, the pyridone compound represented by the formula:



(wherein X¹, X², X³, A¹, A², A³, R¹⁷ and R¹⁸ have the same meanings as defined above), a salt thereof or hydrates thereof. The further preferable mode includes the compound, a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ are hydrogen atoms in the above formula (III); namely, 1,3,5-substituted pyridone compound represented by the formula:



(wherein X¹, X², X³, A¹, A² and A³ have the same meanings as defined above), a salt thereof or hydrates thereof. The most preferable mode includes the compound, a salt thereof or hydrates thereof, wherein X¹, X² and X³ are single bonds in the above formula (IV); namely, 1,3,5-substituted pyridone compound represented by the formula:



(wherein A¹, A² and A³ have the same meanings as defined above), a salt thereof or hydrates thereof. The preferable

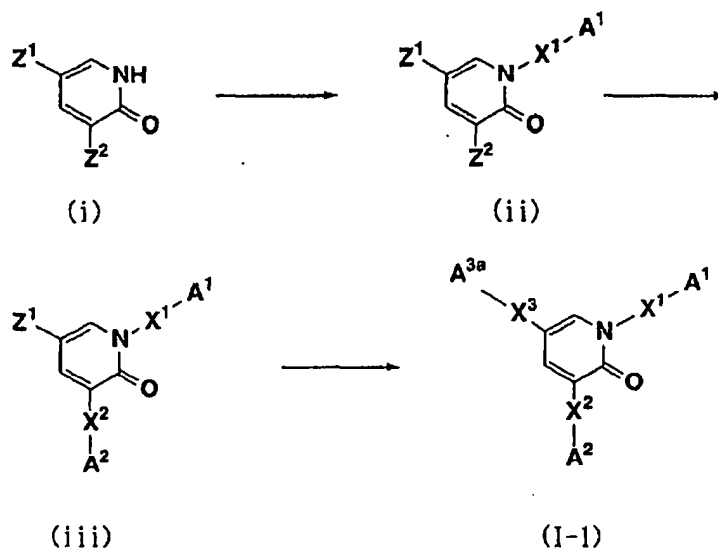
groups in A¹, A² and A³ are as in the above exemplification.

[0046] There is no particular limitation for "a salt" in the specification of the present application so far as it forms a salt with the compound of the present invention and is a pharmacologically acceptable one. Preferably, salt with a hydrogen halide (such as hydrofluoride, hydrochloride, hydrobromide or hydroiodide), salt with an inorganic acid (such as sulfate, nitrate, perchlorate, phosphate, carbonate or bicarbonate), salt with an organic carboxylic acid (such as acetate, trifluoroacetate, oxalate, maleate, tartrate, fumarate or citrate), salt with an organic sulfonic acid (such as methanesulfonate, trifluoromethanesulfonate, ethanesulfonate, benzenesulfonate, toluenesulfonate or camphorsulfonate), salt with an amino acid (such as aspartate or glutamate), salt with a quaternary amine, salt with an alkaline metal (such as sodium salt or potassium salt) and salt with an alkaline earth metal (such as magnesium salt or calcium salt). More preferred examples of the "pharmacologically acceptable salt" are hydrochloride, oxalate etc.

[0047] Representative manufacturing methods for the compounds represented by the above formula (I) according to the present invention will be illustrated as hereunder.

Production process 1

[0048]

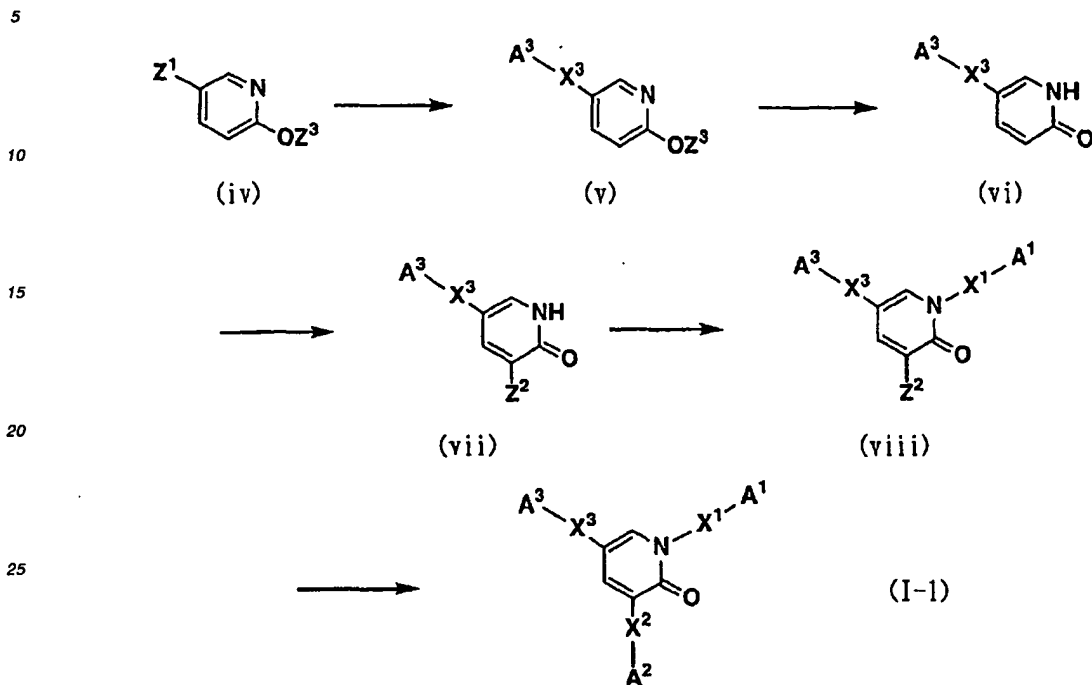


Wherein A¹, A² and A³ may be the same as or different from each other and each indicates optionally substituted C₃₋₈ cycloalkyl group, the C₃₋₈ cycloalkenyl group, 5- to 14-membered non-aromatic heterocyclic group, C₆₋₁₄ aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group; Z¹ and Z² are the same as or different from each other and each represents halogen atoms; and X¹, X² and X³ have the same meanings as defined above. In the present production process, the most preferable A¹, A² and A³ are optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group. The above-mentioned production process 1 is a process of producing the compound (I-1) which is related to the present invention, by introducing A¹, A² and A³ in the pyridone compound which has the substituents Z¹ and Z². Namely, the compound (I-1) which is related to the present invention can be produced by the process that the pyridone compound (i) which has the substituents Z¹ and Z² and an aryl boronic acid derivative are provided to a coupling reaction using a copper compound to obtain the compound (ii), and then A² and A³ are introduced in the compound (ii) by carrying out the coupling reaction with an organometallic reagent using a transition metal catalyst or an organoboron compound, preferably carrying out the coupling reaction with an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative, using a palladium catalyst. The preferable aryl boronic acid derivative which is used for the reaction of producing the compound (ii) differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but the aryl boronic acid derivative which has a group corresponding to A¹ introduced as an aryl group, such as preferably a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted, or the like, can be used. Preferable result can be also obtained by the present reaction in the

presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. When the base is used in the coupling reaction of the present reaction, it is not specifically limited, and preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di- μ -hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride, and the like. The more preferable result can be obtained by carrying out the reaction of producing the compound (ii) from (i) in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited so long as it is inert to the reaction and dissolves the raw material in a certain amount. Preferably, dichloromethane, tetrahydrofuran, ethyl acetate and the like may be proposed. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The aryl tin compound, the aryl zinc compound or the aryl boronic acid derivative which is used for the reaction of producing the compound (I-1) by introducing A² and A³ in the compound (ii) differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but a phenyl tin compound which may be optionally substituted, a heterocyclic tin compound which may be optionally substituted, a phenyl zinc compound which may be optionally substituted, a heterocyclic zinc compound which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, an aryl tin compound, an aryl zinc compound or an aryl boronic acid derivative which has a group corresponding to A² or A³ introduced as an aryl group, can be preferably used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, it is not specifically limited, unless the reaction is not disturbed, and preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited in usual, and known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. The reaction of producing the compound (I-1) by introducing A² and A³ in the compound (ii) is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property, and the solvent used is not specifically limited in usual, but dimethylformamide, toluene, xylene, benzene and the like are preferably mentioned. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. In addition to them, the compound (I-1) related to the present invention can be also produced by the process that the pyridone compound (iii) after introduction of A¹ and A^{2a} is introduced to an organoboron compound or an organometallic reagent, preferably a boronic acid derivative, a tin compound or a zinc compound, and the derivative is provided to a coupling reaction with a halogenated aryl derivative using a transition metal catalyst, preferably a palladium catalyst.

Production process 2

[0049]

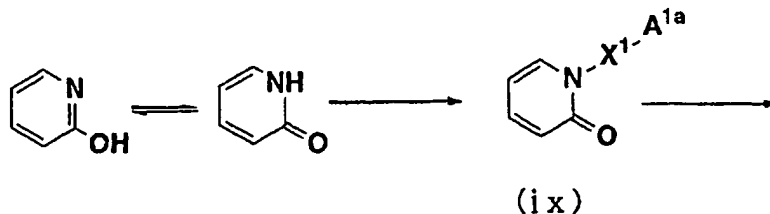


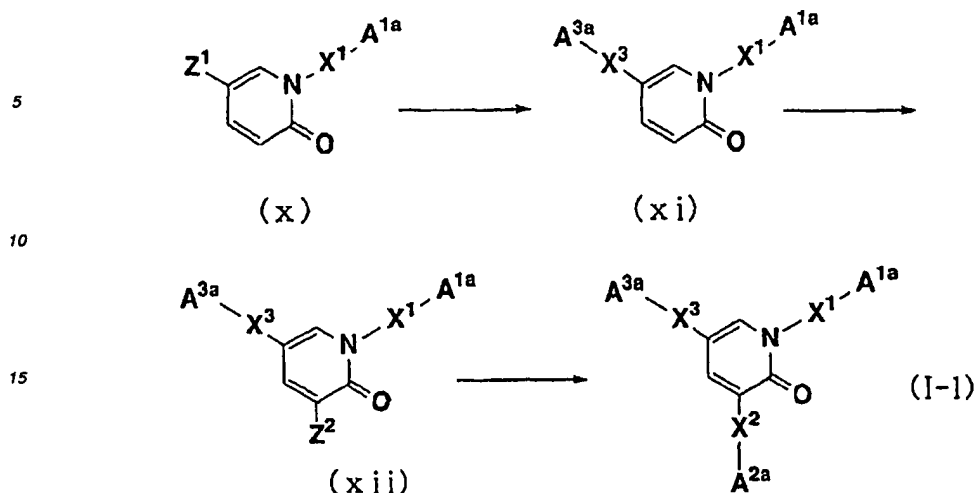
Wherein X^1 , X^2 , X^3 , A^1 , A^2 , A^3 , Z^1 and Z^2 indicate the same meanings as defined above; and Z^3 indicates a protecting group of hydroxy group of an alcohol (for example, a C_{1-6} alkyl group, a benzyl group and the like). In the present production process, the most preferable A^1 , A^2 and A^3 are optionally substituted C_{6-14} aromatic hydrocarbocyclic group or 5- to 14-membered aromatic heterocyclic group. The compound (I-1) according to the present invention can be also produced by introducing A^1 , A^2 and A^3 to the pyridine compound (IV) having substituents Z^1 and $-OZ^3$. The reaction of producing the compound (V) by introducing A^3 to the compound (iv) can be carried out by providing to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing the compound (iv) to the coupling reaction with an aryl tin derivative, an aryl zinc derivative, or an aryl boronic acid derivative in the presence of a base, using a palladium catalyst. The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative used for the present reaction differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative which has a group corresponding to A^3 introduced as an aryl group, can be preferably used. The base used differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited in usual, and known palladium complex such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. Further, the present reaction is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting material, a solvent used and the like, and those which dissolve the starting material to a certain degree are not specifically limited unless the reaction is not disturbed, but dimethylformamide, toluene, xylene, benzene and the like are preferably mentioned. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the pyridone compound (vi) by de-protecting of Z^3 can be carried out by some known processes, and for example, a conventional process described in T.W. Greene and P.G.M. Wuts "Protecting groups in organic synthesis 2nd Edition (1991)" is mentioned as the representative process. The reaction of producing the pyridone compound (vii) by introducing the substituent Z^2 to the compound (vi) can be usually carried out by a

known halogenation method. The halogenating agent differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like are preferably used. The compound (viii) can be produced by providing the compound (vii) and an aryl boronic acid derivative to the coupling reaction using a copper compound and by introducing A¹. The aryl boronic acid derivative used is not specifically limited in usual, and an aryl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted, and an aryl boronic acid derivative which has a group corresponding to A¹ introduced as an aryl group, can be used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically limited, and preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited so long as it is inert to the reaction and dissolves the starting materials in a certain amount, but is preferably dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The final step of producing the compound (I-1) related to the present invention can be carried out by providing the compound (viii) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing to the coupling reaction with an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative using a palladium catalyst, and by introducing A² to the compound (viii). The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative which is used is not specifically limited usually, and a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative which has a group corresponding to A² introduced as an aryl group, can be preferably used. The sequential reaction of producing (I-1) from (viii) which was mentioned in the production process 2 can also obtain a preferable result in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, it is not specifically limited, unless the reaction is not disturbed, and preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited in usual, and known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. Further, a more preferable result can be obtained by carrying out the present reaction in the presence of a solvent, and the solvent used is not specifically limited in usual, and the solvent used differs depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. In addition to them, the compound (I-1) related to the present invention can be also produced by the process that the pyridone compound (viii) after introduction of A^{1a} is introduced to an organoboron compound or an organometallic reagent, preferably a boronic acid derivative, a tin compound or a zinc compound, and the derivative is provided to a coupling reaction with a halogenated aryl derivative using a transition metal catalyst, preferably a palladium catalyst.

Production process 3

[0050]



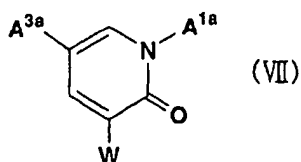


Wherein X¹, X², X³, A¹, A², A³, Z¹ and Z² have the same meanings as defined above, and each of the most preferable group of A¹, A² and A³ in the present production process is the C₆₋₁₄ aromatic hydrocarbocyclic group or the 5 to 14 membered aromatic heterocyclic group which may optionally have substituents, respectively. The compound (I-1) according to the present invention can be also produced by introducing A¹, A² and A³ to 2-hydroxypyridine. The reaction of producing the compound (ix) can be conducted by providing an aryl boronic acid derivative to the coupling reaction using a copper compound, the Ullmann reaction with a halogenated aryl derivative, or a substitution reaction for the halogenated aryl derivative and by introducing A¹ to 2-hydroxypyridine. The aryl boronic acid derivative used in the coupling reaction differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited unless the reaction is not disturbed. The aryl boronic acid derivative having a group corresponding to A¹ introduced as an aryl group such as a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted, and the like can be preferably used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically limited unless the reaction is not disturbed, but is preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine) copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The Ullmann reaction is carried out at 60°C to under refluxing by heating, preferably 100 to 200°C in the presence of a base such as potassium carbonate, sodium carbonate or sodium acetate, using copper or a copper compound such as copper iodide, copper chloride, copper bromide or the like, which is not specifically limited usually. The solvent used differs depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, tetralin, dichlorobenzene, nitrobenzene and the like. The substitution reaction with the halogenated aryl derivative is not specifically limited, but carried out under ice-cooling to under refluxing by heating, preferably at room temperature to 60°C in a solvent such as tetrahydrofuran or dimethylformamide or the like, using a base such as potassium carbonate, sodium hydride, potassium hydride, sodium butoxide, or potassium butoxide or the like. The reaction of producing the compound (x) by introducing the substituent Z¹ to the compound (ix) can be usually carried out by known halogenation method. The halogenating agent used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited, unless the reaction is not disturbed, but a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like are preferably used. The reaction of producing the compound (xi) by introducing A³ to the compound (x) can be usually carried out by providing the compound (x) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing it to the coupling reaction with an aryl tin derivative, an aryl zinc derivative, or an aryl boronic acid

derivative in the presence of a base, using a palladium catalyst. The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative which is used for the present reaction is not specifically limited usually, but an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative having a group corresponding to A³ introduced as an aryl group such as a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, can be preferably used. The base used differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited in usual, and known palladium catalysts such as tetrakis(triphenyl)phosphine palladium and the like are preferably mentioned. Further, the present reaction is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the compound (xii) by introducing the substituent Z² to the compound (xi) can be usually carried out by known halogenation method. The halogenating agent used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited, unless the reaction is not disturbed, but a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like are preferably used. The final step of producing the compound (I-1) related to the present invention can be carried out by providing the compound (xii) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing it to the coupling reaction with an aryl tin derivative, an aryl zinc derivative or an aryl boronic acid derivative using a palladium catalyst, and by introducing A² to the compound (xii). The aryl tin derivative, the aryl zinc derivative or the aryl boronic acid derivative which is used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed. The aryl tin derivative, aryl zinc derivative or aryl boronic acid derivative having a group corresponding to A^{2a} introduced as an aryl group, such as a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted, can be used. At this time, the base used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but known palladium catalysts such as tetrakis(triphenyl)phosphine palladium and the like are mentioned. Further, a more preferable result can be obtained by carrying out the present reaction in the presence of a solvent, and the solvent used is not specifically limited in usual, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. In addition to them, the compound (I-1) related to the present invention can be also produced by the process that the compound (xii) is introduced to an organoboron compound or an organometallic reagent, preferably a boronic acid derivative, a tin compound or a zinc compound or the like, and the derivative is provided to a coupling reaction with a halogenated aryl derivative using a transition metal catalyst, preferably a palladium catalyst.

operation property and stirring property. The solvent used differs depending on a starting material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the compound (xv) by introducing the substituent A³ to the compound (xiv) can be carried out by providing the compound (xiv) to the coupling reaction with an organometallic reagent or an organoboron compound using a transition metal catalyst, preferably by providing it to the coupling reaction with an aryl tin compound, aryl zinc compound, or aryl boronic acid derivative in the presence of a base, using a palladium catalyst. The aryl tin compound, aryl zinc compound or aryl boronic acid derivative used in the present reaction differs usually depending on a starting raw material, a reagent and the like, and is not specifically limited unless the reaction is not disturbed. The aryl tin compound, aryl zinc compound or aryl boronic acid derivative having a group corresponding to A³ introduced as an aryl group, such as a phenyl tin derivative which may be optionally substituted, a heterocyclic tin derivative which may be optionally substituted, a phenyl zinc derivative which may be optionally substituted, a heterocyclic zinc derivative which may be optionally substituted, a phenyl boronic acid derivative, a heterocyclic boronic acid derivative which may be optionally substituted and the like can be preferably used. The base used differs depending on a starting raw material, a solvent used and the like and is not specifically limited unless the reaction is not disturbed, but is preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. The palladium catalyst used is not specifically limited usually, but known palladium catalysts such as tetrakis(triphenylphosphine) palladium and the like are preferably mentioned. Further, the present reaction is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C. The reaction of producing the pyridone compound (xvi) by de-protecting the removal of Z³ can be carried out by some known processes, and for example, a conventional process described in T.W.Greene and P.G.M.Wuts "Protecting groups in organic synthesis 2nd Edition (1991)" is mentioned as the representative process. The final step of producing the compound (I-1) related to the present invention can be conducted by providing the compound (xvi) and an aryl boronic acid derivative to the coupling reaction using a copper compound, the Ullmann reaction with a halogenated aryl derivative, or a substitution reaction for the halogenated aryl derivative and by introducing A¹. The aryl boronic acid derivative used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed. The aryl boronic acid derivative having a group corresponding to A¹ introduced as an aryl group, such as a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted and the like can be used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically limited unless the reaction is not disturbed, but is preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine) copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby. The Ullmann reaction is carried out at 60°C to under refluxing by heating, preferably 100 to 200°C in the presence of a base such as potassium carbonate, sodium carbonate or sodium acetate, using copper or a copper compound such as copper iodide, copper chloride, copper bromide or the like, which is not specifically limited usually. The solvent used differs depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably dimethylformamide, toluene, xylene, tetralin, dichlorobenzene, nitrobenzene and the like. The substitution reaction with the halogenated aryl derivative is not specifically limited, but carried out under ice-cooling to under refluxing by heating, preferably at room temperature to 60°C in a solvent such as tetrahydrofuran or dimethylformamide or the like, using a base such as potassium carbonate, sodium hydride, potassium hydride, sodium butoxide, or potassium butoxide or the like.

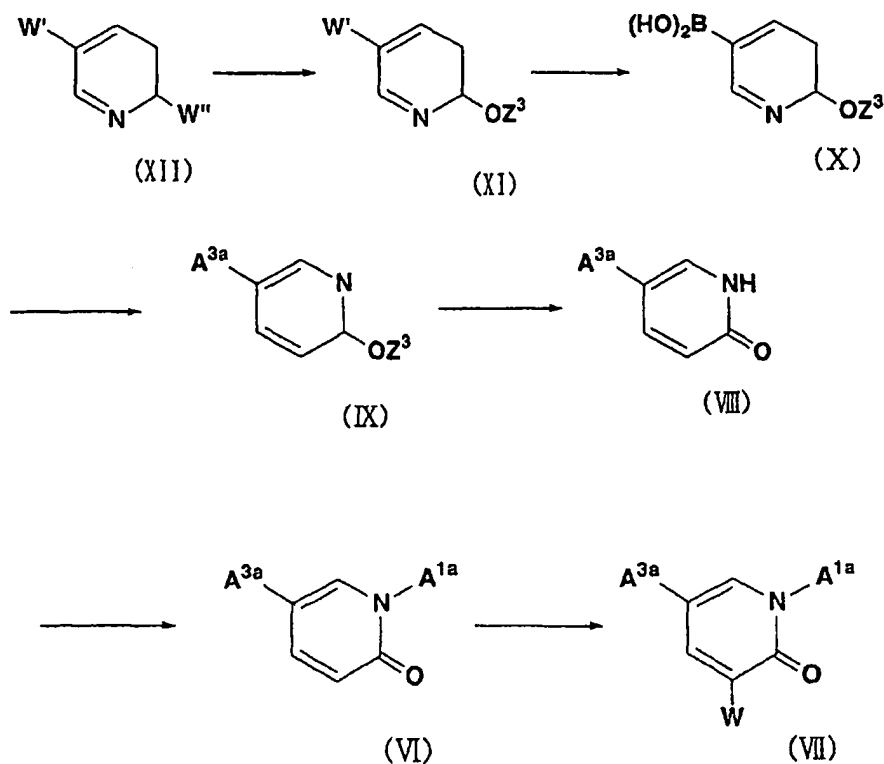
[0053] In the above production process, the production intermediate represented by the formula:



10 (wherein A^{1a}, A^{3a} and W have the same meanings as defined above) can be also produced by the following method (Production process 5).

Production process 5

15 [0054]



[0055] W, W' and W'' in the above formula indicate the same or different halogen atom, and the most preferable atom is bromine atom.

[0056] The compound (XII) can be easily produced according to known methods or corresponding methods, and further, can be easily obtained as a commercially available substance. The step of producing the compound (XI) from the compound (XII) is a step of reacting the compound (XII) with the base represented by the formula Z³OM (M indicates an alkali metal atom). The base differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably sodium alkoxide, and preferably sodium methoxide, sodium ethoxide and the like in particular. In this case, it is preferable to carry out the reaction in an alcohol corresponding to the alkoxide used, and for example, it is preferable to carry out in methanol in case of using sodium methoxide and ethanol in case of using sodium ethoxide, etc.

[0057] The step of producing the compound (X) from the compound (XI) is a step of reacting the compound (XI) with trimethoxyborane in the presence of a base. The base used differs depending on a starting raw material, a solvent

used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably n-butyllithium and the like. The solvent used differs depending on a starting raw material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably ethers such as tetrahydrofuran, and the like. When n-butyllithium is used as a base, the reaction can be terminated by an acid such as hydrochloric acid, or the like according to a conventional method.

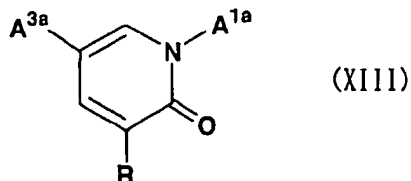
[0058] The step of producing the compound (IX) from the compound (X) is a step of carrying out the coupling reaction of the compound (X) with a halogenoaryl or a halogenoheteroaryl which corresponds to the substituent A^{3a} introduced, in the presence of a base and a palladium catalyst and producing the compound (IX). The palladium catalyst used is not specifically limited, but palladium acetate/triphenylphosphine catalyst and the like can be mentioned as the preferable example. The base used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably cesium carbonate, sodium carbonate, potassium carbonate, and the like. Further, the present step is preferably carried out in the presence of a solvent from the viewpoints of operation property and stirring property. The solvent used differs depending on a starting raw material, a solvent used and the like, and the solvent which does not disturb the reaction and dissolves the starting material to a certain degree is not specifically limited, but is preferably 1,2-dimethoxyethane, dimethylformamide, toluene, xylene, benzene and the like. The reaction temperature is not specifically limited, and usually room temperature, or under refluxing by heating, and preferably 50 to 160°C.

[0059] The step of producing the compound (VIII) from the compound (IX) is a step of submitting to the reaction of protecting the removal of Z³ of the compound (IX). The present step can be carried out by some known processes, and for example, a method of refluxing the compound (IX) by heating in the presence of an acid (preferably, hydrochloric acid and the like) is mentioned. Additionally, for example, a conventional process described in T.W.Greene and P.G.M.Wuts "Protecting groups in organic synthesis 2nd Edition (1991)" is mentioned as the representative process.

[0060] The step of producing the compound (VI) from the compound (VIII) is a step of submitting the compound (VIII) and the aryl boronic acid derivative represented by the formula A^{1a}B(OH)₂ to the coupling reaction using a copper compound and introducing A^{1a}. The aryl boronic acid derivative used is not specifically limited usually. The aryl boronic acid derivative which has a group corresponding to A^{1a} introduced as an aryl group, such as a phenyl boronic acid derivative which may be optionally substituted, a heterocyclic boronic acid derivative which may be optionally substituted and the like can be used. Preferable result can be also obtained by the present reaction in the presence of a base, and at this time, the base used differs depending on a starting raw material, a solvent used and the like. Further, the base is not specifically limited unless the reaction is not disturbed, but is preferably triethylamine, pyridine, tetramethylethylenediamine and the like. Preferable examples of the copper compound used include copper acetate, di-μ-hydroxobis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride, and the like. Further, the present reaction is preferably carried out in the presence of a solvent. The solvent used differs usually depending on a starting raw material, a reagent and the like, and the solvent which does not disturb the reaction and dissolves the starting raw material to a certain degree is not specifically limited, but is preferably N,N-dimethylformamide, dichloromethane, tetrahydrofuran, ethyl acetate and the like. Further, the present reaction is preferably carried out under atmosphere of oxygen or in air flow, and good results (the reduction of the reaction time and the improvement of yield etc.) can be obtained thereby.

[0061] The step of producing the compound (VII) from the compound (VI) is a step of submitting the compound (VI) to the halogenation reaction. The halogenation reaction can be usually carried out by known halogenation methods. The halogenating agent used differs depending on a starting raw material, a solvent used and the like, and is not specifically limited unless the reaction is not disturbed, but is preferably a bromination agent such as acetic acid-bromine, N-bromosuccinimide or the like, an iodination agent such as iodine, N-iodosuccinimide or the like, and the like.

[0062] According to the above production process 5, the production intermediates (VI) and (VII) can be produced in high yield. Further, when the production intermediates the production intermediates of the compounds related to the present invention are produced according to the production processes, the contamination of a copper compound to the final product can be easily prevented, and the compounds of the present invention satisfying the point of safety (toxicity and the like) can be provided. Accordingly, the production processes are extremely excellent production processes from the viewpoints of yield and safety, experimentally and industrially. The novel compound represented by the formula:

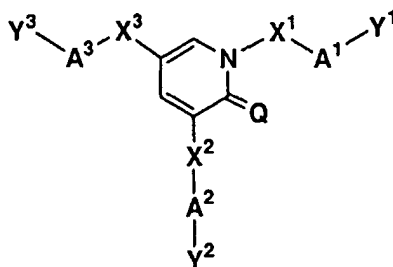


10 (wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates a C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14 membered aromatic heterocyclic group which may optionally have a substituent, respectively; and R indicates hydrogen atom or a halogen atom) or a salt thereof is useful as the production intermediate in the production of the compound (I) according to the present invention or a salt thereof. In the formula (XIII), the preferable examples

15 in A^{1a} and A^{3a} may be the same as or different from each other, and each includes phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group etc., which may optionally have substituents, respectively. The more preferable examples may be the same as or different from each other, and each includes a phenyl group, pyridyl group, pyrimidinyl group,

20 thienyl group, furyl group etc., which may optionally have substituents, respectively. Further, the preferable examples in R in particular are hydrogen atom or bromine atom.

[0063] The substituents on A¹, A² and A³ in the compound represented by the formula:



35 (wherein Q, X¹, X², X³, A¹, A² and A³ have the same meanings as defined above; Y¹, Y² and Y³ indicates the same or different substituents; and each of the most preferable group in A¹, A² and A³ is a C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14 membered aromatic heterocyclic group which may optionally have substituents, respectively) can be converted by various reactions. For example, the representative processes are as below. That is, various reactions

40 are known for changing to a functional group from a nitro group when (1) Y¹, Y² and/or Y³ are/is nitro group(s) and, although there is no particular limitation for the method and for the resulting substance, a method of changing to an amine derivative by a reduction reaction may be exemplified. Although there is usually no particular limitation for the reduction condition, preferred conditions are a method where iron, zinc or tin is used under acidic conditions, a hydrogenation method where palladium, rhodium, ruthenium, platinum or a complex thereof is used as a catalyst. When the amine derivative produced by the said reduction reaction is used, it is possible to further change to an amide compound,

45 a carbamate compound, a sulfonamide compound, a halogen compound, a substituted amine compound etc., easily. (2) When Y¹, Y² and/or Y³ are/is alkoxy group(s), an example for changing to a functional group from an alkoxy group is a method to change to an alcohol derivative by means of deprotection. The alcohol derivative which is prepared by the said method may be easily changed to an ester compound by a dehydrating condensation with carboxylic acid derivative or by a reaction with an acid chloride or may be easily changed to an ether compound by a Mitsunobu reaction or by a condensation reaction with a halogen compound. (3) When Y¹, Y² and/or Y³ are/is aldehyde group

50 (s), various reactions are known for changing to a functional group from an aldehyde group and, although there is no particular limitation for the method therefor and the resulting substance by the change, an example is a method of changing to a carboxylic acid derivative by an oxidation reaction. The carboxylic acid derivative prepared by the said method may be easily changed further to an ester compound, a ketone compound, etc. In addition, starting from the said carboxylic acid derivative, it is possible to easily manufacture an alcohol derivative by a reduction reaction, an amine derivative by a reductive amination reaction, a secondary alcohol compound by an addition reaction with an organic metal reagent and various alkyl derivatives by a Wittig reaction. (4) When Y¹, Y² and/or Y³ are/is halogen atom

55

(s), an example for changing to a functional group from a halogen atom as a substituent is a method of changing to a nitrile derivative by a substitution reaction. Besides the above, it is also possible to easily change to various kinds of compounds via, for example, an organolithium compound, an organomagnesium compound, an organotin compound or an organoboronic acid derivative etc.

5 [0064] The above-mentioned methods is the method for the manufacture of the compound (I) of the present invention. The starting compound in the above-mentioned methods may form a salt or a hydrate and there is no particular limitation for such salt and hydrate so far as they do not inhibit the reaction. When the compound (I) of the present invention is obtained in a free substance, it may be changed to a state of a salt by conventional methods. Further, various isomers (for example, a geometrical isomer, an enantiomer based on an asymmetric carbon, a rotamer, a stereoisomer, a tautomer, and the like) which are obtained for the compound (I) related to the present invention are purified by using
10 usual separation procedures, for example, such as recrystallization, a diastereomer salt method, an enzymolysis method, various chromatographies (for example, thin layer chromatography, column chromatography, gas chromatography, and the like), and can be separated.

[0065] The compound of the present invention represented by the above formula (I), a salt thereof or hydrates thereof
15 may be made into pharmaceutical preparations such as tablets, diluted powder, fine granules, granules, coated tablets, capsules, syrup, troche, inhalation preparation, suppositories, injections, ointments, eye ointments, eye drops, nasal preparations, ear drops, cataplasma or lotions by means of conventional methods. In the manufacture of the pharmaceutical preparations, it is possible to use commonly used fillers, binders, disintegrating agent, lubricants, coloring agents, corrigents and, if necessary, stabilizers, emulsifiers, absorption promoters, surfactant, pH adjusting agents,
20 antiseptics, antioxidants, etc. and, after compounding with the ingredients commonly used as materials for the pharmaceutical preparations, it is made into pharmaceutical preparations by a common method. Examples of the components therefor are 1) animal and plant oil such as soybean oil, beef tallow or synthetic glyceride; 2) hydrocarbon such as liquid paraffin, squalane or solid paraffin; 3) ester oil such as octyldodecyl myristate or isopropyl myristate; 4) higher alcohol such as cetostearyl alcohol or behenyl alcohol; 5) silicone resin; 6) silicone oil; 7) surfactant such as polyoxyethylene fatty acid ester, sorbitan fatty acid ester, glycerol fatty acid ester, polyoxyethylene sorbitan fatty acid ester,
25 polyoxyethylene hydrogenated castor oil or polyoxyethylene-polyoxypropylene block copolymer; 8) water-soluble high-molecular substance such as hydroxyethyl cellulose, polyacrylic acid, carboxyvinyl polymer, polyethylene glycol, polyvinylpyrrolidone or methylcellulose; 9) lower alcohol such as ethanol or isopropanol; 10) polyhydric alcohol such as glycerol, propylene glycol, dipropylene glycol or sorbitol; 11) saccharide such as glucose or sucrose; 12) inorganic powder such as silicic acid anhydride, aluminum magnesium silicate or aluminum silicate; 13) pure water and the like. Applicable examples of (1) a filler are lactose, corn starch, pure sugar, glucose, mannitol, sorbitol, crystalline cellulose, silicon dioxide etc.; those of (2) a binder are polyvinyl alcohol, polyvinyl ether, methyl cellulose, ethyl cellulose, gum arabic, tragacanth, gelatin, shellac, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, polypropylene glycol-polyoxyethylene block copolymer, meglumine, calcium citrate, dextrin, pectin etc.; those of (3) a disintegrating agent are starch, agar, gelatin powder, crystalline cellulose, calcium carbonate, sodium bicarbonate, calcium citrate, dextrin, pectin, carboxymethyl cellulose calcium etc.; those of (4) a lubricant are magnesium stearate, talc, polyethylene glycol, silica, hydrogenated plant oil etc.; those of (5) a coloring agent are those which are allowed to add to pharmaceuticals; those of (6) a corrigent are cocoa powder, menthol, aromatic powder, peppermint oil, borneol and cinnamon powder; and those of (7) an antioxidant are those which are permitted to be added to pharmaceuticals, such
35 as ascorbic acid, α -tocopherol and the like, are respectively used.

[0066] (1) In the manufacture of preparations for oral use, the compound of the present invention or a pharmacologically acceptable salt is mixed with a filler and, if necessary, further with a binder, a disintegrating agent, a lubricant, a coloring agent, a corrigent, etc. and the mixture is made into diluted powder, fine particles, granules, tablets, coated tablets, capsules, etc. by a common method. (2) In case of tablets and coated tablets, there is of course no problem that such tablets and granules are sugar-coated, gelatin-coated, or appropriately coated upon necessity. (3) In case
45 of the manufacture of liquid preparations such as syrup, injection preparations and eye drops, a pH adjusting agent, a solubilizer, an isotonicizing agent, etc. and, if necessary, a solubilizing aid, a stabilizer, buffer, suspending agent, antioxidant etc. are added, and then made into pharmaceutical preparations by a common method. It can be made as a freeze drying product, and a injections can be dosed in vena, subcutis, and muscle. Preferable examples in a suspending agent include methyl cellulose, polysorbate 80, hydroxyethyl cellulose, gum arabic, tragacanth powder, sodium carboxymethyl cellulose, polyoxyethylene sorbitan monolaurate, and the like; preferable examples in a resolving aid include polyoxyethylene hardened castor oil, polysorbate 80, nicotinic acid amide, polyoxyethylene sorbitan monolaurate, and the like; preferable examples in a stabilizer include sodium sulfite, meta sodium sulfite, ether, and the like; preferable examples in a preservative include methyl p-oxybenzoate, ethyl p-oxybenzoate, sorbic acid, phenol, cresol,
50 chlorocresol and the like. Further, (4) in case of external use, there is no particular limitation for a method of manufacturing a pharmaceutical preparation, but a common method is used for the manufacture. Thus, with regard to a base material used, various materials which are commonly used for pharmaceuticals, quasi drugs, cosmetics, etc. may be used. Specific examples of the base material used are animal/plant oil, mineral oil, ester oil, waxes, higher alcohols,

fatty acids, silicone oil, surfactant, phospholipids, alcohols, polyhydric alcohols, water-soluble high-molecular substances, clay minerals and pure water and, if necessary, it is possible to add pH adjusting agent, antioxidant, chelating agent, antiseptic antifungal, coloring agent, perfume, etc. If necessary, it is further possible to compound other components such as a component having a differentiation-inducing action, blood flow promoter, bactericide, anti-inflammatory agent, cell activator, vitamins, amino acid, moisturizer and keratin solubilizing agent.

[0067] Dose of the pharmaceutical agent according to the present invention varies depending upon degree of symptom, age, sex, body weight, dosage form, type of salt, sensitivity to the pharmaceuticals, specific type of the disease, etc. and, in the case of adults, the daily dose is usually about 30 μ g to 10 g, preferably, 100 μ g to 5 g or, more preferably, 100 μ g to 100 mg in the case of oral administration while, in the case of administration by injection, it is usually about 30 μ g to 1 g, preferably 100 μ g to 500 mg or, more preferably, 100 μ g to 30 mg. That is administered once daily or in several portions a day.

[0068] In accordance with the present invention, it is possible to provide a novel compound (I) which show an excellent inhibiting action to AMPA receptor and/or kainate receptor and are useful as pharmaceutical agents. Further, a useful production process for producing the compound or its salt and a production intermediate could be provided. According to this process, the compound relating to the present invention can be obtained in high yield, and the highly safe compound can be obtained. The compound (I) of the present invention suppress the neurotoxicity of excitatory neurotransmitters and is able to achieve an excellent neuroprotecting action as a pharmaceutical agent. Accordingly, the compounds of the present invention are useful as therapeutic, preventive and improving agents for various nervous diseases and are useful, for example, as therapeutic and preventive agents for acute neurodegenerative diseases (such as cerebrovascular disorders at acute stage, subarachnoid hemorrhag, head injury, spinal cord injury, neuropathy caused by hypoxia or hypoglycemia etc.), chronic neurodegenerative diseases (such as Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis or spinocerebellar degeneration), epilepsy, hepatic encephalopathy, peripheral neuropathy, Parkinson's syndrome, spasticity, pain, neuralgia, schizophrenia, anxiety, drug abuse, nausea, vomiting, urinary disturbance, visual disturbance due to glaucoma, auditory disturbance due to antibiotics, food poisoning, infectious cerebrospinal meningitis (such as HIV cerebrospinal meningitis), cerebrovascular dementia, or dementia or nervous symptoms due to meningitis. Further, the compound of the present invention is useful as an agent for treating or preventing demyelinating disorder (such as encephalitis, acute disseminated encephalomyelitis, multiple sclerosis, acute demyelinating polyneuropathy, Guillain Barre syndrome, chronic inflammatory demyelinating polyneuropathy, Marchifava-Bignami disease, central pontine myelinolysis, neuromyelitis optica, Devic syndrome, Balo disease, HIV-myelopathy, HTLV-myelopathy, progressive multifocal leucoencephalopathy and a secondary demyelinating disorder (such as CNS lupus erythematoses, polyarteritis nodosa, Sjogren syndrome, sarcoidosis and isolated cerebral vasculitis)).

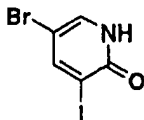
Examples

[0069] The following Reference Examples, Examples and Test Examples are exemplary, and not intended to limit the present invention. One skilled in the art may make various variations of Reference Examples, Examples and Test Examples as well as claims of the invention to fully utilize the invention. These variations shall be included in claims of the invention.

Referential Example 1

5-Bromo-3-iodo-1,2-dihydropyridin-2-one

[0070]

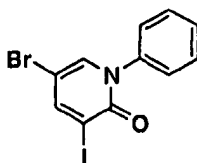


[0071] 2-Amino-5-bromopyridine (CAS No. 1072-97-5) (300 g) was dissolved in a mixed solvent consisting of 1000 ml of acetic acid and 200 ml of water, 30 ml of concentrated sulfuric acid were gradually dropped thereto under stirring. Then, 79.1 g of periodic acid hydrate and 176 g of iodine were added thereto, followed by stirring at 80°C for 4 hours. To the reaction mixture were added periodic acid hydrate (40g) and iodine (22g), followed by further stirring

at 80°C for 2 hours. After cooling to room temperature, the reaction mixture was poured onto ice (3000ml) and neutralized to pH 7.0 with 5N aqueous sodium hydroxide. The resulting crystals were collected by filtration, dissolved in a mixed solvent of ethyl acetate/diethyl ether, successively washed with aqueous sodium thiosulfate, water, 1N aqueous sodium hydroxide and brine, and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, to give 392g of 2-amino-5-bromo-3-iodopyridine (yield: 76%). 2-Amino-5-bromo-3-iodopyridine (100 g) was gradually added to 300 ml of concentrated sulfuric acid under ice-cooling. After the reaction mixture was stirred at room temperature for 2 hours, it was ice-cooled again. 35 g of sodium nitrite were gradually added thereto, followed by stirring at room temperature for 3 days and nights. The reaction solution was poured onto ice (3000 ml) and neutralized to pH 4.0 with sodium hydroxide. The resulting crystals were collected by filtration, washed with water and warm air-dried at 60°C for one day and night, to give 102 g (quantitative) of the title compound. ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.60 (d, 1H) , 8.14 (d, 1H). Referential Example 2.

5-Bromo-1-phenyl-3-iodo-1,2-dihydropyridin-2-one

[0072]



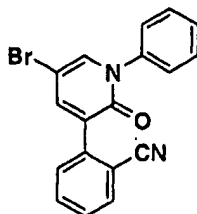
[0073] 5-Bromo-3-iodo-1,2-dihydropyridin-2-one (10.0 g) obtained in Referential Example 1, 10.0 g of phenylboronic acid and 8.1 g of copper acetate were suspended in 500 ml of dichloromethane. 15 ml of triethylamine were added thereto, followed by stirring at room temperature for 5 days and nights. To the reaction solution were added 200 ml of water and 50 ml of aqueous ammonia, followed by stirring vigorously. Then the insoluble matters were filtered off through Celite, the filtrate was extracted with dichloromethane, the extract was dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was recrystallized from ethyl acetate/hexane, to give 6.54 g (yield: 52%) of the title compound.

¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.34-7.38 (m, 2H), 7.44-7.52 (m, 3H), 7.53 (d, 1H), 8.10 (d, 1H).

Referential Example 3.

5-Bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0074]



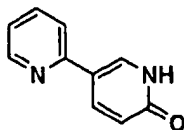
[0075] 5-Bromo-1-phenyl-3-iodo-1,2-dihydropyridin-2-one (11.69 g) obtained in Referential Example 2, 8.0 g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate and 16.0 g of cesium carbonate were suspended in 150 ml of dimethylformamide. 3.0 g of tetrakis(triphenyl)phosphine palladium were added thereto, followed by stirring at 80°C in nitrogen atmosphere for 2 hours. The reaction solution was poured into water, the mixture was extracted with ethyl acetate, the extract was successively washed with water and brine and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, and the residue was purified by a silica gel column chromatography (hexane/ethyl acetate system), followed by recrystallizing from ethyl acetate/hexane, to give 5.67 g (yield: 52%) of the title compound.

¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.42-7.54 (m, 6H), 7.61-7.65 (m, 4H), 7.66 (d, 1H), 7.74-7.77 (m, 1H).

Referential Example 4.

5-(2-Pyridyl)-1,2-dihydropyridin-2-one

[0076]

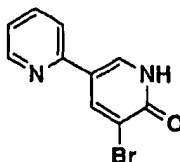


[0077] 2,5-Dibromopyridine [CAS No. 624-28-2] (400 g) was added to 3500 ml of a 28% methanolic solution of sodium methoxide, the mixture was stirred at 60°C for 3 hours and allowed to cool, the reaction solution was poured into 3 liters of water, the mixture was extracted with 9000 ml of diethyl ether, the extract was washed with a saturated saline solution for three times and dried over anhydrous magnesium sulfate and the solvent was evaporated *in vacuo*. The residue was dissolved in 2 liters of dimethylformamide, 900 g of tri-N-butyl-(2-pyridyl) tin [CAS No. 59020-10-9] and 20 g of tetrakis(triphenylphosphine) palladium and mixture was stirred at 120°C in a nitrogen atmosphere for 3 hours. The reaction solution was allowed to cool and poured into 3 liters of water, the mixture was extracted with 10 liters of diethyl ether, the extract was successively washed with a saturated sodium bicarbonate solution and a saturated saline solution and the solvent was evaporated *in vacuo*. A 48% aqueous solution (800 ml) of hydrogen bromide was added to the residue and the mixture was stirred at 110°C for 3 hours. After allowing to cool, the reaction solution was washed with 3 liters of diethyl ether, poured into 2 liters of ice, adjusted to pH 11.0 with a 5N sodium hydroxide solution and washed with 3 liters of diethyl ether again. The aqueous layer was adjusted to pH 7.0 and extracted with dichloromethane. The crude crystals prepared by evaporating the solvent *in vacuo* were washed with a mixed solvent consisting of diethyl ether and hexane to give 201.5 g (yield: 69%) of the title compound. ¹H-NMR (400MHz, CDCl₃); δ (ppm) 6.72 (d, 1H), 7.20 (ddd, 1H), 7.50-7.54 (m, 1H), 7.73 (dt, 1H), 8.12-8.15 (m, 1H), 8.19 (dd, 1H), 8.60-8.64 (m, 1H).

Referential Example 5.

3-Bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one

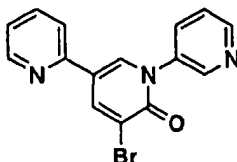
[0078]



[0079] 5-(2-Pyridyl)-1,2-dihydropyridin-2-one (201.5 g) obtained in Referential Example 4 was dissolved in 1300 ml of dimethylformamide, 208.3 g of N-bromosuccinimide were added thereto and the mixture was stirred at room temperature for 2 hours. The reaction mixture was poured into 4 liters of ice water and the precipitate was filtered and dried with warm air at 50°C for two days and nights to give 230 g (yield: 79%) of the title compound. ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.21-7.26 (m, 1H), 7.52 (d, 1H), 7.75 (dt, 1H), 8.21 (d, 1H), 8.61-8.64 (m, 1H), 8.67 (d, 1H). Referential Example 6.

3-Bromo-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0080]



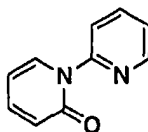
[0081] Dichloromethane (300 ml) was added to 18.75 g of 3-bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one obtained in Referential Example 5 and 18.36 of 3-pyridineboronic acid, then 3.47 g of di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine) copper (II)] chloride were added and the mixture was stirred in an oxygen atmosphere for 4 days and nights. The reaction solution was purified by an NH silica gel short column (eluted by ethyl acetate), the solvent was evaporated in *vacuo* and the resulting crude crystals were washed with diethyl ether to give 24.26 g (yield: 99%) of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.23-7.26(m, 1H), 7.47-7.51(m, 1H), 7.52-7.56(m, 1H), 7.77 (dt, 1H), 7.87-7.91 (m, 1H), 8.19 (d, 1H), 8.53 (d, 1H), 8.59-8.62 (m, 1H), 8.71-8.75 (m, 2H).

Referential Example 7.

1-(2-Pyridyl)-1,2-dihydropyridin-2-one

[0082]



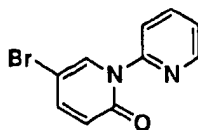
[0083] 25ml of a dimethylformamide solution containing 4.00g of 2(1H)-pyridone and 8.00g of 2-bromopyridine was incorporated with 3.80g of potassium carbonate and 0.51g of cuprous iodide, followed by stirring at 120°C for 2 hours. After the mixture was returned to room temperature, water was added thereto. The mixture was extracted with ethyl acetate, and the ethyl acetate layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:1), to give 1.58g of the title compound as a pale yellow wax.

¹H-NMR(400MHz, CDCl₃); δ(ppm) 6.31(dt, 1H), 6.67(d, 1H), 7.33(ddd, 1H), 7.40(ddd, 1H), 7.82-7.90(m, 2H), 7.96(dd, 1H), 8.57(dd, 1H).

Referential Example 8.

1-(2-Pyridyl)-5-bromo-1,2-dihydropyridin-2-one

[0084]



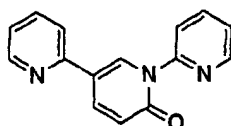
[0085] Under ice-cooling, 15ml of a dimethylformamide solution containing 1.50g of 1-(2-pyridyl)-1,2-dihydropyridin-2-one was incorporated with 1.60g of N-bromosuccinic acid imide. The mixture was stirred at room temperature for 2 hours, and then diluted with water and extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:3), to give 1.13g of the title compound as a pale brown powder.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.57(d, 1H), 7.34(ddd, 1H), 7.42(dd, 1H), 7.85(dt, 1H), 7.97(dd, 1H), 8.10(d, 1H), 8.57(dd, 1H).

Referential Example 9.

1-(2-Pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0086]



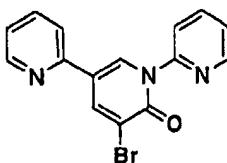
[0087] 2.5ml of a dimethylformamide solution containing 0.10g of 1-(2-Pyridyl)-5-bromo-1,2-dihydropyridin-2-one and 0.30g of 2-tributyl stannyl pyridine was incorporated with 0.05g of dichlorobis(triphenyl)phosphine palladium, followed by stirring at 130°C for 2 hours. The mixture was returned to room temperature, followed by diluting with water and extracting with ethyl acetate. The organic layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate), to give 0.076g of the title compound as a pale yellow powder.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.77(d, 1H), 7.22(dd, 1H), 7.36(dd, 1H), 7.61(d, 1H), 7.76(dt, 1H), 7.87(dt, 1H), 7.97(d, 1H), 8.12(dd, 1H), 8.60-8.65(m, 2H), 8.67(d, 1H).

Referential Example 10.

1-(2-Pyridyl)-5-(2-pyridyl)-3-bromo-1,2-dihydropyridin-2-one

[0088]



[0089] 2ml of a dimethylformamide solution containing 0.07g of 1-(2-pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one was incorporated with 0.07g of N-bromosuccinic acid imide, under stirring and ice-cooling. After stirring the mixture at room temperature for 2 hours, it was diluted with water and extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=3:1), to give 0.05g of the title compound as a pale brown powder.

¹H-NMR(400MHz, DMSO-d₆); δ(ppm) 7.33(ddd, 1H), 7.58(ddd, 1H), 7.83-7.88(m, 2H), 7.97(dd, 1H), 8.07(dt, 1H), 8.59-8.62(m, 1H), 8.65-8.80(m, 1H), 8.72(d, 1H), 8.81(d, 1H).

Referential Example 11.

3,5-Dibromo-2-methoxypyridine

[0090]



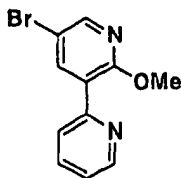
[0091] 80ml of a 28% sodium methoxide solution was incorporated with 30.0g of 2,3,5-tribromopyridine under ice-cooling, followed by stirring at 50°C for 2 hours. The reaction solution was diluted with water and extracted with diethyl ether. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:20), to give 18.5g of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.99(s,3H), 7.93(d,1H), 8.14(d,1H).

Referential Example 12.

3-(2-Pyridyl)-5-bromo-2-methoxypyridine

[0092]



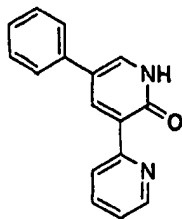
[0093] 100ml of a dimethylformamide solution containing 6.3g of 3,5-dibromo-2-methoxypyridine and 8.1g of 2-tributyl stannyl pyridine was incorporated with 1.0g of tetrakis(triphenylphosphine) palladium, followed by stirring at 120°C for 2 hours in nitrogen atmosphere. After the mixture was returned to room temperature, the solvent was evaporated, and the residue was extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane=1:3), to give 2.8g of the title compound as a pale yellow powder.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.02(s,3H), 7.31(dd,1H), 7.80(dt,1H), 8.02(ddd,1H), 8.25(d,1H), 8.40(d,1H), 8.71-8.74(m,1H).

Referential Example 13.

3-(2-Pyridyl)-5-phenyl-2-(1H)-pyridone

[0094]



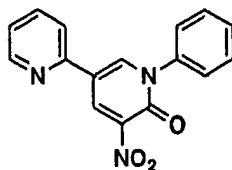
[0095] A mixture of 1.0g of 3-(2-pyridyl)-5-bromo-2-methoxypyridine, 0.9g of phenylboronic acid, 0.3g of dichlorobis(triphenylphosphine) palladium and 2ml of triethylamine was stirred at 120°C for 1.5 hours in 30ml of xylene in nitrogen atmosphere. The mixture was returned to room temperature, diluted with ethyl acetate, washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated, and the residue was incorporated with 47% hydrobromic acid and heated at 70°C for 1 hour. The reaction solution was ice-cooled, diluted with water, and neutralized with potassium carbonate. The resulting precipitates were collected by filtration, washed with water and ether, and then air-dried, to give 0.5g of the title compound as a pale yellow powder.

¹H-NMR(400MHz, DMSO-d₆); δ(ppm) 7.30-7.37(m, 2H), 7.43(dd, 2H), 7.62(d, 2H), 7.82-7.90(m, 1H), 7.87(d, 1H), 8.64-8.69(m, 2H), 8.57(d, 1H), 12.30(brs, 1H).

Referential Example 14.

1-Phenyl-3-nitro-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0096]



(14a) 3-Nitro-1-phenyl-1,2-dihydropyridin-2-one

[0097] 5g of 2-hydroxy-3-nitropyridine, 7.14g of phenylboronic acid, 2.6g of copper (II) acetate, 9.9ml of triethylamine and 5.8ml of pyridine were added to 100ml of tetrahydrofuran, followed by stirring overnight. The reaction mixture was poured into aqueous ammonia, and extracted with ethyl acetate. The organic layer was washed with water, dried, and concentrated. The residue was suspended into ether, and collected by filtration, to give 4.71g of the title compound. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.39(dd, 1H), 7.36-7.40(m, 2H), 7.49-7.54(m, 3H), 7.73(dd, 1H), 8.38(dd, 1H).

(14b) 5-Bromo-3-nitro-1-phenyl-1,2-dihydropyridin-2-one

[0098] 10ml of a dimethylformamide solution containing 1g of 3-nitro-1-phenyl-1,2-dihydropyridin-2-one was incorporated with 988mg of N-bromosuccinimide, followed by stirring at room temperature overnight. Further, it was stirred at 50°C for 3 hours. The reaction mixture was poured into ice-water, and the resulting precipitates were collected by filtration, to give 1.27g of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.36-7.39(m, 2H), 7.50-7.57(m, 3H), 7.88(d, 1H), 8.42(d, 1H).

(14c) 3-Nitro-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

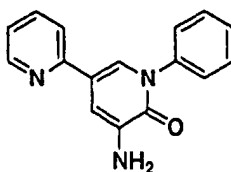
[0099] 1.27g of 5-bromo-3-nitro-1-phenyl-1,2-dihydropyridin-2-one, 2.38g of 2-tri-n-butyl stannyl pyridine and 248mg of tetrakis(triphenyl)phosphine palladium were added to 20ml of xylene, followed by stirring at 120°C overnight in nitrogen atmosphere. The reaction mixture was purified by silica gel chromatography (ethyl acetate/hexane system), to give 638mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.28(ddd, 1H), 7.45-7.63(m, 6H), 7.80(dt, 1H), 8.61(ddd, 1H), 8.63(d, 1H), 9.03(d, 1H).

Referential Example 15.

3-Amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0100]



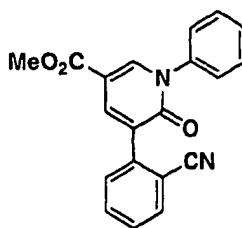
[0101] 100mg of 10% palladium-carbon was added to 20ml of an ethanol solution containing 546mg of 3-nitro-1-phenyl-5-(pyridin-2-yl)-1,2-dihydropyridin-2-one, followed by stirring overnight in hydrogen atmosphere. The reaction mixture was filtered through silica gel and concentrated, to give 411mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.36-4.42(m, 1H), 7.18(dd, 1H), 7.28(d, 1H), 7.44-7.54(m, 6H), 7.61(d, 1H), 7.70(dt, 1H), 8.57-8.60(m, 1H).

Referential Example 16.

3-(2-Cyanophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one

[0102]



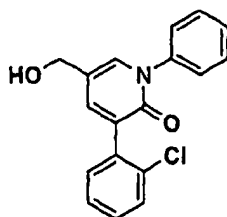
[0103] 6g of methyl 5-bromo-6-hydroxynicotinate synthesized by a known method from 6-hydroxynicotinic acid, and 6.3g of phenylboronic acid were dissolved in 200ml of tetrahydrofuran. To the mixture were added 939mg of copper acetate and 1ml of pyridine, followed by stirring at room temperature for 3 nights. Aqueous ammonia was added to the reaction solution, and the solution was extracted with chloroform. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue obtained as a solid was washed with diethyl ether, to give 7.35g of 3-bromo-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one as white crystals. 5g of the product was dissolved in 100ml of dimethylformamide, followed by adding 4.6g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 7.9g of cesium carbonate and 375mg of tetrakis(triphenyl)phosphine palladium, and stirring at 140°C for 1 hour in nitrogen atmosphere. After cooling to room temperature, the reaction mixture was poured into water, and extracted with ethyl acetate. Then, the extract was successively washed with water and brine, and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 3.23g of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.89(s, 3H), 7.42-7.55(m, 6H), 7.61-7.66(m, 2H), 7.75(dd, 1H), 8.14(d, 1H), 8.35

(d, 1H). Referential Example 17.

3-(2-Chlorophenyl)-5-hydroxymethyl-1-phenyl-1,2-dihydropyridin-2-one

[0104]

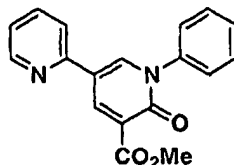


[0105] 36mg of 3-(2-chlorophenyl)-5-methoxycarbonyl-1-phenyl-1,2-dihydropyridin-2-one synthesized by the method of Referential Example 3 from 3-bromo-5-methoxycarbonyl-1-phenyl-1,2-dihydropyridin-2-one and 2-chloroboronic acid, was dissolved in 20ml of toluene. After cooling to -78°C, 0.1ml diisopropyl aluminum hydride (1.5M tetrahydrofuran solution) was added dropwise thereto. While heating from -78°C to room temperature, the mixture was stirred overnight. Then, 1N hydrochloric acid was added thereto, followed by stirring. The mixture was neutralized with an aqueous solution of sodium hydrogen carbonate, and then extracted with ethyl acetate. Then, the extract was successively washed with water and brine, and dried over anhydrous magnesium sulfate. Then, the solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 12mg of the title compound. ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 4.48 (s, 2H), 7.25-7.29 (m, 3H), 7.37-7.51 (m, 8H). ESI-Mass; 312 [M⁺+H]

Referential Example 18.

3-Methoxycarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0106]

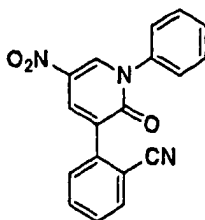


[0107] 4.5g of methyl 5-bromo-2-hydroxynicotinate synthesized by a known method from 2-hydroxynicotinic acid, and 4.7g of phenylboronic acid were dissolved in 200ml of tetrahydrofuran. To the mixture were added 705mg of copper acetate and 1ml of pyridine, followed by stirring at room temperature for 3 nights in a flow of air. Aqueous ammonia was added to the reaction solution, and the solution was extracted with chloroform. The organic layer was washed with brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue obtained as a solid was washed with diethyl ether, to obtain 3.59g of 5-bromo-3-methoxycarbonyl-1-phenyl-1,2-dihydropyridin-2-one as white crystals. 3.2g of the product was dissolved in 100ml of dimethylformamide, to which 7.7g of tri-N-butyl-(2-pyridyl) tin [CAS No.59020-10-9] and 240mg of tetrakis(triphenyl)phosphine palladium were added, followed by stirring at 110°C for 3 hours in nitrogen atmosphere. After cooling to room temperature, the reaction solution was poured into water, extracted with ethyl acetate. Then, the extract was successively washed with water and brine, dried over anhydrous magnesium sulfate, and then filtered through NH silica gel and silica gel. Then, the filtrate was evaporated, and the resulting precipitates were washed with ether and hexane, and dried, to give 1.59g of the title compound. ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 3.95 (s, 3H), 7.22 (ddd, 1H), 7.42-7.54 (m, 5H), 7.62 (dt, 1H), 7.76 (td, 1H), 8.52 (d, 1H), 8.58 (ddd, 1H), 8.85 (d, 1H).

Referential Example 19.

3-(2-Cyanophenyl)-5-nitro-1-phenyl-1,2-dihydropyridin-2-one

[0108]



(19a) 5-Nitro-1-phenyl-1,2-dihydropyridin-2-one

[0109] 5.93g of the title compound was obtained in accordance with the method used for Referential Example (14-1), from 5g of 2-hydroxy-5-nitropyridine.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 6.67(d, 1H), 7.39-7.43(m, 2H), 7.53-7.59(m, 3H), 8.18(dd, 1H), 8.68(dd, 1H).

(19b) 3-Bromo-5-nitro-1-phenyl-1,2-dihydropyridin-2-one

[0110] 4.72g of the title compound was obtained in accordance with the method used for Referential Example (14-2), from 5.93g of 5-nitro-1-phenyl-1,2-dihydropyridin-2-one.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.38-7.42(m, 2H), 7.54-7.58(m, 3H), 8.59-8.61(m, 1H), 8.66-8.68(m, 1H).

(19c) 5-Nitro-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

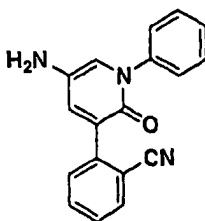
[0111] 758mg of the title compound was obtained in accordance with the method used for Referential Example 3, from 3g of 3-bromo-5-nitro-1-phenyl-1,2-dihydropyridin-2-one.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.47-7.63(m, 7H), 7.68(dt, 1H), 7.80(ddd, 1H), 8.38(d, 1H), 8.78(d, 1H).

Referential Example 20.

5-Amino-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0112]



[0113] 414mg of the title compound was obtained in accordance with the method used for Referential Example 15, from 708mg of 5-nitro-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 6.99(d, 1H), 7.39-7.49(m, 7H), 7.60(dt, 1H), 7.73(d, 1H), 7.75(d, 1H).

EP 1 300 396 A1

Example 1.

3-(2-Cyanophenyl)-5-(2-nitrophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0114] 5-Bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one (100 mg), 60 mg of 2-nitrophenylboronic acid and 130 mg of cesium carbonate were suspended in 10 ml of dimethylformamide, then 20 mg of tetrakis(triphenylphosphine) palladium were added and the mixture was stirred at 120°C in a nitrogen atmosphere for 4 hours. After allowing to cool, the reaction solution was poured into water, the mixture was extracted with ethyl acetate, the extract was dried over anhydrous magnesium sulfate, the solvent was evaporated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 35 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ(ppm) 7.40-7.80 (m, 14H), 7.97 (dd, 1H).

Example 2.

5-(2-Aminophenyl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0115] 3-(2-Cyanophenyl)-5-(2-nitrophenyl)-1-phenyl-1,2-dihydropyridin-2-one (32 mg) was dissolved in 15 ml of ethyl acetate, 5 mg of 10% palladium-carbon (water-containing substance) were added and the mixture was stirred at room temperature in a hydrogen atmosphere for 15 minutes. The catalyst was filtered off and the solvent was evaporated *in vacuo* to give 20 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ(ppm) 3.95 (bs, 2H), 6.76 (dd, 1H), 6.80 (dt, 1H), 7.14 (dd, 1H), 7.17 (dt, 1H), 7.41-7.55 (m, 6H), 7.59 (d, 1H), 7.62 (dt, 1H), 7.74-7.82 (m, 2H), 7.88 (d, 1H).

Example 3.

3-(2-Cyanophenyl)-5-(2-methylsulfonylamino-phenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0116] 5-(2-Aminophenyl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one (16 mg) was dissolved in 10 ml of dimethylformamide, then 0.05 ml of triethylamine and 3 drops of methanesulfonyl chloride were added and the mixture was stirred at room temperature for one hour. Ethyl acetate was added to the reaction solution, the mixture was washed with water and a saturated saline solution, the solvent was evaporated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 5 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ(ppm) 2.19 (s, 3H), 6.88-6.95 (m, 1H), 7.08-7.15 (m, 1H), 7.38-7.55 (m, 8H), 7.61 (dt, 1H), 7.69-7.76 (m, 3H), 7.91 (d, 1H), 7.92-7.97 (m, 1H).

Example 4.

3-(2-Chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

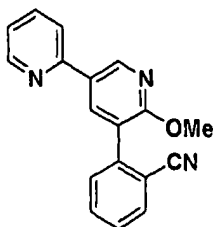
[0117] 3-Iodo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one (200 mg) synthesized by the same method as mentioned in Referential Example 6, 130 mg of 2-chloro-3-pyridyl boronic acid and 250 mg of cesium carbonate were suspended in 10 ml of dimethylformamide, 40 mg of tetrakis(triphenylphosphine) palladium were added and the mixture was stirred at 100°C in a nitrogen atmosphere for 3 hours. After allowing to cool, the reaction solution was poured into water, the mixture was extracted with ethyl acetate, the extract was dried over anhydrous magnesium sulfate, the solvent was evaporated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 143 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ(ppm) 7.20-7.24 (m, 1H), 7.31 (dd, 1H), 7.44-7.59 (m, 6H), 7.75 (dt, 1H), 7.91 (dd, 1H), 8.25 (d, 1H), 8.33 (d, 1H), 8.41 (dd, 1H), 8.59-9.62 (m, 1H).

Example 5.

3-(2-Cyanophenyl)-5-(2-pyridyl)-2-methoxypyridine

[0118]



[0119] Tetrakis(triphenyl)phosphine palladium (0.15 g) was added to a mixed solution of 0.50 g of 5-(2-pyridyl)-3-bromo-2-methoxypyridine, 0.42 g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 0.82 g of cesium carbonate and 20 ml of dimethylformamide and the mixture was stirred at 140°C in a nitrogen atmosphere for 5 hours. After cooling to room temperature, ethyl acetate was added thereto, the mixture was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (ethyl acetate:hexane = 1:3) to give 0.36 g of the title compound as pale yellow powder.

¹H-NMR (CDCl₃, 400MHz); δ (ppm) 4.03 (3H, s), 7.24-7.28 (1H, m), 7.46-7.51 (1H, ddd), 7.57 (1H, dd), 7.65-7.69 (1H, ddd), 7.72-7.82 (3H, m), 8.31 (1H, d), 8.66-8.69 (1H, m), 8.83 (1H, d).

Example 6.

3-(2-Cyanophenyl)-5-(2-pyridyl)-2(1H)-pyridone

[0120] Chlorotrimethylsilane (0.1 ml) was added to a suspension of 0.20 g of 3-(2-cyanophenyl)-5-(2-pyridyl)-2-methoxypyridine and 0.12 g of sodium iodide in 10 ml of acetonitrile and the mixture was stirred at room temperature for 3 hours. A saturated sodium bicarbonate solution was added to the mixture followed by extracting with ethyl acetate. The ethyl acetate layer was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (ethyl acetate:hexane = 1:1) to give 0.11 g of the title compound in pale yellow powder.

¹H-NMR (DMSO-d₆, 400 MHz); δ (ppm) 7.26-7.30 (1H, ddd), 7.55-7.60 (1H, ddd), 7.66 (1H, dd), 7.74-7.79 (1H, ddd), 7.80-7.86 (1H, ddd), 7.89-7.94 (2H, m), 8.28 (1H, d), 8.37 (1H, d), 8.56-8.59 (1H, m).

Example 7.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0121] A suspension of 0.11 g of 3-(2-cyanophenyl)-5-(2-pyridyl)-2(1H)-pyridone, 0.12 g of phenyl boronic acid, 0.1 g of copper acetate and 0.3 ml of triethylamine in 10 ml of methylene chloride was stirred at room temperature for overnight. To this were added 5 ml of concentrated aqueous ammonia, 10 ml of water and 40 ml of ethyl acetate and the organic layer was separated, washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (ethyl acetate:hexane = 1:2) to give 0.06 g of the title product as pale yellow powder.

¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 7.29-7.33 (1H, m), 7.48-7.63 (6H, m), 7.71-7.75 (1H, dd), 7.76-7.88 (2H, m), 7.92-7.95 (1H, m), 8.01 (1H, d), 8.48 (1H, d), 8.54 (1H, d), 8.58-8.61 (1H, m).

Example 8.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one

[0122] The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.24-7.28 (m, 1H), 7.49 (dt, 1H), 7.63-7.81 (m, 6H), 7.95-7.98 (m, 1H), 8.31-8.37

(m,3H), 8.45(t,1H), 8.60-8.63(m,1H).

Example 9.

5 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one

[0123] Iron powder (180 mg) and 342 mg of ammonium chloride were added to a solution of 317 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one in a mixture of 10 ml of 2-propanol and 5 ml of water followed by refluxing for 4 hours. The reaction mixture was concentrated, partitioned in ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 235 mg of the title compound as a pale yellow solid.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 3.84 (s, 2H), 6.75 (dd, 1H), 6.82-6.87 (m, 2H), 7.20 (dd, 1H), 7.26-7.30 (m, 1H), 7.45 (td, 1H), 7.59-7.65(m,2H), 7.72-7.80(m,3H), 8.29(s,2H), 8.56-8.61(m,1H)

15 Example 10.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminophenyl)-1,2-dihydropyridin-2-one

[0124] Triethylamine (0.2 ml) was added to a solution of 31 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 2 ml of tetrahydrofuran, 0.1 ml of methanesulfonic acid chloride was dropped therein with ice cooling and the mixture was stirred for 10 minutes. To this were added 2 ml of 2N sodium hydroxide, the mixture was stirred at room temperature for 5 minutes and partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate-hexane system) to give 38 mg of the title compound as a pale yellow amorphous substance. ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.22-7.31 (m, 3H), 7.36 (t, 1H), 7.43 (t, 1H), 7.46 (dd, 1H), 7.61 (dt, 1H), 7.65 (td, 1H), 7.73-7.78 (m, 3H), 8.27 (d, 1H), 8.31 (d, 1H), 8.59-8.61 (m, 1H) .

Example 11.

30 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminophenyl)-1,2-dihydropyridin-2-one

[0125] Paraformaldehyde (41 mg) and 119 mg of triacetoxysodium borohydride were added to a solution of 50 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 3 ml of acetic acid followed by stirring at room temperature for one night. To this was added an aqueous solution of sodium bicarbonate, the mixture was extracted with ethyl acetate, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 11 mg of the title compound as a pale yellow solid.

¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 2.00 (s, 3H), 7.11-7.14 (m, 1H), 7.21 (ddd, 1H), 7.35 (t, 1H), 7.44-7.49 (m, 2H), 7.59 (d, 1H), 7.66 (td, 1H), 7.70-7.77 (m, 4H), 8.25 (d, 1H), 8.51 (s, 1H), 8.58-8.61 (m, 1H).

Example 12.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-dimethylaminophenyl)-1,2-dihydropyridin-2-one

[0126] Paraformaldehyde (41 mg) and 119 mg of triacetoxysodium borohydride were added to a solution of 50 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 3 ml of acetic acid followed by stirring at room temperature for 6 hours. To this were further added 41 mg of paraformaldehyde and 119 mg of triacetoxysodium borohydride, the mixture was stirred for one night, an aqueous solution of sodium bicarbonate was added thereto, the mixture was extracted with ethyl acetate, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 38 mg of the title compound as a pale yellow amorphous substance.

¹H-NMR (400MHz,CDCl₃) ; δ(ppm) 2.99 (s, 6H), 6.77-6.80 (m, 3H), 7.18-7.21(m,1H), 7.32-7.37(m,1H), 7.44(t,1H), 7.59-7.64(m,1H), 7.71-7.83 (m, 3H), 8.32 (s, 2H), 8.58-8.60 (m, 1H).

Example 13.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[3-(5-methoxymethyl-2-oxazolidinon-3-yl)-phenyl]-1,2-dihydropyridin-2-one

[0127] Glycidyl methyl ether (0.01 ml) and 22 mg of magnesium periodate were added to a solution of 38 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one in 6 ml of acetonitrile followed by stirring at room temperature. After 2 hours, 0.01 ml of glycidyl methyl ether and 22 mg of magnesium periodate were further added thereto and the mixture was stirred at room temperature for 1 hours and then stirred at 50°C for 1 hour more. The reaction mixture was partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated, the residue was dissolved in 6 ml of tetrahydrofuran, 32 mg of carbonyldiimidazole were added thereto and the mixture was heated to reflux for 2 hours. This was partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a preparative thin layer chromatography (ethyl acetate/hexane system) to give 21 mg of the title compound as a pale yellow solid.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.43 (s, 3H), 3.64 (dd, 2H), 3.97(dd, 1H), 4.09 (t, 1H), 4.77 (ddd, 1H), 7.22 (ddd, 1H), 7.29 (ddd, 1H), 7.46 (td, 1H), 7.53 (t, 1H), 7.59-7.79 (m, 5H), 8.30 (d, 1H), 8.31 (d, 1H), 8.58-8.61 (m, 1H).

Example 14.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one

[0128] The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.94 (s, 3H), 7.23 (ddd, 1H), 7.47 (td, 1H), 7.59-7.68 (m, 4H), 7.73-7.80 (m, 3H), 7.88-7.91 (m, 2H), 8.31 (d, 1H), 8.32 (d, 1H), 8.59-8.61 (m, 1H).

Example 15.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminocarbonylphenyl)-1,2-dihydropyridin-2-one

[0129] 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one (10 mg) was added to 6 ml of a 40% methanolic solution of methylamine followed by stirring at room temperature for one night. The reaction solution was concentrated *in vacuo* to give 10 mg of the title compound as a pale yellow solid.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.00 (d, 3H), 6.51 (brs, 1H), 7.23 (ddd, 1H), 7.47 (td, 1H), 7.58-7.68 (m, 4H), 7.73-7.80 (m, 3H), 7.88-7.91 (m, 2H), 8.31 (d, 1H), 8.32 (d, 1H), 8.59-8.61 (m, 1H).

Example 16.

3-(2-Cyano-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

(Route 1)

[0130] 3-(2-Chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one (281 mg) was dissolved in 20 ml of dimethylformamide, 170 mg of copper cyanide were added and the mixture was stirred at 130°C for 10 hours. The reaction solution was cooled to room temperature, aqueous ammonia and ethyl acetate were added, the organic layer was partitioned, washed with water and dried over anhydrous sodium sulfate, the drying agent was filtered off, the filtrate was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 120 mg of the title compound as a colorless amorphous substance.

(Route 2)

[0131] 3-Bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one (2.9 g) synthesized by the same method as mentioned in Referential Example 6 was dissolved in 200 ml of xylene, 5 ml of bis(tributyl tin) and 400 mg of tetrakis(triphenyl)phosphine palladium were added and the mixture was stirred at 140°C for 2 hours. 3-Bromo-2-cyanopyridine (3.2 g) and 100 mg of tetrakis(triphenyl)phosphine palladium were added thereto and the mixture was stirred at 140°C for 2 hours.

Tetrakis(triphenyl)phosphine palladium (1.0 g) and 800 mg of copper iodide were divided into four and added every 1 hour, then 2 g of 3-bromo-2-cyanopyridine were added thereto and the mixture was stirred at 140°C for one night. The reaction solution was cooled to room temperature, water and ethyl acetate were added thereto, the organic layer was partitioned, washed with water and dried over anhydrous sodium sulfate, the drying agent was filtered off, the filtrate

was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 1.8 g of the title compound as a colorless amorphous substance.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.24 (ddd, 1H), 7.47-5.57 (m, 6H), 7.63 (d, 1H), 7.68 (td, 1H), 8.22 (dd, 1H), 8.37 (dd, 1H), 8.43 (d, 1H), 8.59-8.61 (m, 1H), 8.69 (dd, 1H).

ESI-Mass; 351 [M⁺ + H]

Example 17.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one

[0132] The title compound was obtained in the same manner as in Example 4.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 3.84 (s, 3H), 6.98-7.03 (m, 2H), 7.19 (ddd, 1H), 7.28-7.33 (m, 2H), 7.40-7.46 (m, 2H), 7.46-7.51 (m, 2H), 7.53-7.57 (m, 1H), 7.72 (ddd, 1H), 8.12 (d, 1H), 8.29 (d, 1H), 8.57-8.61 (m, 1H).

Example 18.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one

[0133] 3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one (440 mg) was dissolved in 5 ml of 48% hydrobromic acid and heated to reflux for 1 hours. After the reaction solution was allowed to cool at room temperature, it was diluted with a saturated aqueous solution of sodium bicarbonate and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated *in vacuo* and purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 292 mg of the title compound.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 6.67-6.73(m,2H), 7.12-7.18(m,2H), 7.19-7.24(m,1H), 7.30-7.38(m,2H), 7.47-7.53 (m,2H), 7.56(d,1H), 7.70 (s, 1H), 7.73 (ddd, 1H), 8.18 (d, 1H), 8.26 (d, 1H), 8.57-8.62 (m, 1H).

Example 19.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4 dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one

[0134] 3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one (82 mg) and 57 mg of N,N-dimethylaminoethyl chloride were dissolved in 2 ml of dimethylformamide, 55 mg of potassium carbonate were added thereto at 60°C and the mixture was stirred for one night. The reaction solution was diluted with water and extracted with ethyl acetate. The organic layer was washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated *in vacuo* and purified by an NH silica gel column chromatography (hexane-ethyl acetate system) to give 27 mg of the title compound.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.55 (s, 6H), 2.76 (t, 2H), 4.11 (t, 2H), 6.99-7.05 (m, 2H), 7.19 (ddd, 1H), 7.26-7.34 (m, 2H), 7.39-7.45(m,2H), 7.45-7.51(m,2H), 7.55(d,1H), 7.72(ddd,1H), 8.12 (d, 1H), 8.28 (d, 1H), 8.57-8.61 (m, 1H).

Example 20.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one

[0135] The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.24 (ddd, 1H), 7.84 (ddd, 1H), 7.63 (d, 1H), 7.66 (ddd, 1H), 7.72 (dd, 1H), 7.75-7.82 (m, 3H), 7.84-7.88 (m, 1H), 8.00 (ddd, 1H), 8.05-8.08 (m, 1H), 8.32 (d, 1H), 8.35 (d, 1H), 8.59-8.62 (m, 1H), 10.08 (s, 1H).

Example 21.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-1,2-dihydropyridin-2-one

[0136] 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one (585 mg) was dissolved in 20 ml of methanol, 260 mg of sodium borohydride were added with ice cooling and the mixture was stirred at room temperature for one night. The reaction solution was diluted with ethyl acetate, washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated *in vacuo* and purified by an NH silica gel column chromatography (ethyl acetate). The resulting crude crystals were re-

crystallized from ethyl acetate-diethyl ether to give 320 mg of the title compound.

¹H-NMR (400 MHz, DMSO-d₆); δ(ppm) 4.60 (d, 2H), 5.37 (t, 1H), 7.29-7.33 (m, 1H), 7.42-7.47 (m, 2H), 7.48-7.55 (m, 2H), 7.59 (ddd, 1H), 7.73 (dd, 1H), 7.78 (dd, 1H), 7.83 (ddd, 1H), 7.94 (dd, 1H), 8.01 (d, 1H), 8.48 (d, 1H), 8.52 (d, 1H), 8.57-8.61 (m, 1H).

Example 22.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-cyanomethylphenyl)-1,2-dihydropyridin-2-one

[0137] 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one (53 mg) was dissolved in 2 ml of tetrahydrofuran, then 60 ml of triethylamine and 20 ml of methanesulfonyl chloride were added thereto with ice cooling and the mixture was stirred at room temperature for 3 hours. The reaction solution was diluted with an aqueous solution of sodium bicarbonate and extracted with ethyl acetate and the extract was dried over anhydrous magnesium sulfate. The drying agent was filtered off, the filtrate was concentrated *in vacuo*, the resulting residue was dissolved in 1 ml of dimethyl sulfoxide, 3 mg of sodium cyanide were added and the mixture was stirred at room temperature for 1 hour. The reaction solution was diluted with ethyl acetate, washed with an aqueous solution of sodium bicarbonate and a saturated saline solution and dried over anhydrous magnesium sulfate. The drying agent was filtered off, the filtrate was concentrated *in vacuo* and the resulting crude crystals were recrystallized from ethyl acetate-diethyl ether-hexane to give 12 mg of the title compound.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.85 (s, 2H), 7.21-7.26 (m, 1H), 7.41-7.81 (m, 10H), 8.29-8.32 (m, 2H), 8.59-8.62 (m, 1H).

[0138] The following compounds were prepared by the same manner as in the above Example 22.

Example 23.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-acetylaminomethylphenyl)-1,2-dihydropyridin-2-one

[0139] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.04 (s, 3H), 4.47-4.52 (m, 2H), 7.22 (ddd, 1H), 7.37-7.53 (m, 5H), 7.61 (d, 1H), 7.65 (ddd, 1H), 7.72-7.81 (m, 3H), 8.28 (d, 1H), 8.31 (d, 1H), 8.59-8.62 (m, 1H).

Example 24.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminomethylphenyl)-1,2-dihydropyridin-2-one

[0140] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.91 (s, 3H), 4.36 (d, 2H), 5.00-5.06 (m, 1H), 7.22 (ddd, 1H), 7.43-7.49 (m, 3H), 7.50-7.55 (m, 2H), 7.61 (ddd, 1H), 7.64 (ddd, 1H), 7.73-7.79 (m, 3H), 8.28-8.31 (m, 2H), 8.60 (ddd, 1H).

Example 25.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-acetoxymethylphenyl)-1,2-dihydropyridin-2-one

[0141] To 56 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one were added 1 ml of acetic anhydride and 1 ml of pyridine and the mixture was stirred at room temperature for one night. The reaction solution was concentrated *in vacuo* and purified by an NH silica gel chromatography (hexane-ethyl acetate system) to give 30 mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.13(s, 3H), 5.18(s, 2H), 7.23(ddd, 1H), 7.44-7.56(m, 5H), 7.60-7.67(m, 2H), 7.73-7.81(m, 3H), 8.30-8.33(m, 2H), 8.59-8.62(m, 1H).

Example 26.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one

[0142] The title compound was obtained in the same manner as in Example 7.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 2.53 (s, 1H), 7.21-7.24 (m, 1H), 7.36-8.79 (m, 10H), 8.28-8.32 (m, 2H), 8.59-8.61 (m, 1H).

Example 27.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one

- 5 [0143] A 70% m-chloroperbenzoic acid (500 mg) was added little by little during 2 hours to a solution of 50 mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one in 4 ml of methylene chloride followed by stirring with ice cooling. A saturated aqueous solution of sodium bicarbonate was added thereto, the mixture was partitioned to ethyl acetate-water, the organic layer was washed with water, dried and concentrated and the residue was purified by a silica gel column chromatography (ethyl acetate/hexane system) to give 5 mg of the title compound as a yellow solid.
- 10 ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.11 (s, 3H), 7.24-7.28 (m, 1H), 7.50 (dt, 1H), 7.61-7.82 (m, 7H), 8.20 (d, 2H), 8.30-8.33 (m, 2H), 8.60-8.63 (m, 1H).

Example 28.

3-(2-Cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 15 [0144] The title compound was prepared according to Example 1.
- ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.29 (d, 1H), 7.42-7.57 (m, 6H), 7.65 (dt, 1H), 7.71 (d, 1H), 7.77-7.82 (m, 3H), 7.85 (d, 1H), 10.10 (s, 1H).
- 20

Example 29.

3-(2-Cyanophenyl)-5-(2-diethylaminomethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 25 [0145] A solution of 20 mg of 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one, 0.1 ml of a 2M solution of diethylamine in tetrahydrofuran and 0.1 ml acetic acid in 2 ml of tetrahydrofuran was stirred at room temperature for 15 minutes, 20 mg of sodium triacetoxyborohydride were added and the mixture was stirred for 3 hours more. A 2N aqueous solution of sodium hydroxide was added thereto, the mixture was extracted with ethyl acetate and the organic layer was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated in vacuo and the residue was purified by an NH silica gel column chromatography to give 15 mg of the title compound as white powder.
- 30 ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 1.38 (t, 6H), 2.99-3.20 (m, 4H), 4.57 (d, 2H), 7.07 (d, 1H), 7.40-7.58 (m, 8H), 7.60-7.67 (m, 2H), 7.77 (d, 1H), 7.87 (d, 1H).
- 35

Example 30.

3-(2-Cyanophenyl)-5-(2-hydroxymethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 40 [0146] Sodium triacetoxyborohydride (10 mg) was added to a solution of 10 mg of 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one in 2 ml of tetrahydrofuran and the mixture was stirred for 1 hour. A 10% aqueous solution of sodium carbonate was added thereto, the mixture was extracted with ethyl acetate and the organic layer was washed with water and a saturated saline solution and dried over magnesium sulfate. The solvent was concentrated *in vacuo* and the residue was purified by an NH silica gel column chromatography to give 8 mg of the title compound as white powder.
- 45 ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 4.86 (s, 2H), 7.11 (d, 1H), 7.33 (d, 1H), 7.42-7.54 (m, 6H), 7.60-7.65 (m, 1H), 7.75 (d, 1H), 7.76-7.79 (m, 1H), 7.81-7.84 (m, 1H), 7.91 (d, 1H).
- MS (ESI): 385 (MH⁺)

50 Example 31.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-benzyl-1,2-dihydropyridin-2-one

- 55 [0147] 3-(2-Cyanophenyl)-5-(2-pyridyl)-2(1H)-pyridone (46 mg), 36 mg of benzyl alcohol and 88 mg of triphenylphosphine were dissolved in 2 ml of tetrahydrofuran, 147 mg of a 40% solution of diethylazo dicarboxylate in toluene were added with ice cooling and the mixture was stirred at room temperature for 1 hour. The reaction solution was concentrated in vacuo and purified by a silica gel chromatography (hexane-ethyl acetate system) to give 12 mg of the title compound.

EP 1 300 396 A1

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 5.33 (s, 2H), 7.18 (ddd, 1H), 7.31-7.40 (m, 3H), 7.42-7.48 (m, 3H), 7.53 (dd, 1H), 7.64 (ddd, 1H), 7.68-7.79 (m, 3H), 8.18 (d, 1H), 8.30 (d, 1H), 8.56-8.60 (m, 1H).

Example 32.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0148] 3-Bromo-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one (5.39 g) was dissolved in 200 ml of dimethylformamide, then 6.42 g of cesium carbonate, 3.69 g of 2-(2'-cyanophenyl)-1,3,2-dioxaboronate and 949 mg of tetrakis(triphenylphosphine) palladium were added thereto and the mixture was stirred at 120°C for 1 hour. The reaction solution was cooled to room temperature, water and ethyl acetate were added thereto, the organic layer was partitioned, washed with water and dried over anhydrous magnesium sulfate, the drying agent was filtered off, the filtrate was concentrated *in vacuo* and the residue was purified by a silica gel column chromatography (hexane-ethyl acetate system) to give 4.8 g of the title compound as a colorless amorphous substance.

¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.22-7.26 (m, 1H), 7.46-7.52 (m, 2H), 7.62 (dt, 1H), 7.66 (td, 1H), 7.74-7.81 (m, 3H), 7.97 (ddd, 1H), 8.32 (s, 2H), 8.61 (ddd, 1H), 8.72 (dd, 1H), 8.80-8.81 (m, 1H).

ESI-Mass; 351 [M⁺ + H]

[0149] The following compounds were synthesized by the same method as mentioned in Example 1.

Example 33.

3-(2-Pyridyl)-5-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0150] ¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.35-7.40 (1H, m), 7.49-7.64 (5H, m), 7.77-7.81 (2H, m), 7.86 (1H, dt), 7.96 (1H, d), 8.22 (1H, d), 8.51 (1H, d), 8.66-8.71 (2H, m).

Example 34.

3-(2-Cyanophenyl)-5-(3-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0151] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.38 (dd, 1H), 7.45-7.58 (m, 6H), 7.65 (ddd, 1H), 7.72 (d, 1H), 7.77-7.86 (m, 3H), 7.94 (d, 1H), 8.60 (dd, 1H), 8.79 (d, 1H).

Example 35.

3-(2-Cyanophenyl)-5-(4-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0152] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.44 (dd, 2H), 7.46-7.58 (m, 6H), 7.66 (ddd, 1H), 7.81 (dd, 2H), 7.84 (d, 1H), 8.01 (d, 1H), 8.66 (dd, 2H).

Example 36.

3-(2-Cyanophenyl)-5-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0153] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.26-7.59 (m, 7H), 7.62-7.72 (m, 3H), 7.76-7.80 (m, 2H), 7.82-7.84 (m, 1H), 7.86-7.88 (m, 2H).

ESI-Mass; 374 [M⁺ + H]

Example 37.

3,5-Diphenyl-1-(2-pyridyl)-1,2-dihydropyridin-2-one

[0154] ¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.36-7.40 (3H, m), 7.41-7.47 (4H, m), 7.52-7.56 (2H, m), 7.74-7.78 (2H, m), 7.84-7.90 (2H, m), 7.98-8.01 (1H, m), 8.11 (1H, d), 8.61-8.63 (1H, m).

EP 1 300 396 A1

Example 38.

3-Phenyl-5-(2-cyanophenyl)-1-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0155] ¹H-NMR (400 MHz, DMSO-d₆) ; δ (ppm) 7.34-7.40 (2H, m) , 7.40-7.50 (3H, m) , 7.53 (2H, dd) , 7.67 (1H, dt) , 7.75-7.81 (2H, m), 7.83 (1H, d), 7.88 (1H, dt), 8.02 (1H, d), 8.15 (1H, d), 8.59-8.62 (1H, m).

Example 39.

10 3-(2-Cyanophenyl)-5-phenyl-1-(2-pyridyl)-1,2-dihydropyridin-2-one

[0156] ¹H-NMR (400 MHz, DMSO-d₆) ; δ (ppm) 7.33-7.40 (2H, m), 7.41-7.50 (3H, m), 7.54-7.59 (2H, m), 7.65 (1H, dt), 7.75 (1H, dd), 7.80 (1H, dd), 7.88 (1H, dt), 7.96 (1H, d), 8.03 (1H, d), 8.23 (1H, d), 8.60-8.64 (1H, m).

15 Example 40.

3-(2-Cyanophenyl)-5-(2-cyanophenyl)-1-(2-pyridyl)-1,2-dihydropyridin-2-one

20 [0157] ¹H-NMR (400 MHz, DMSO-d₆) ; δ (ppm) 7.36-7.40 (1H, m), 7.45-7.51 (2H, m), 7.61-7.66 (1H, m), 7.66-7.71 (2H, m), 7.75-7.80 (3H, m), 7.86-7.91 (2H, m), 8.05-8.09 (1H, m), 8.34 (1H, d), 8.59-8.62 (1H, m).

Example 41.

25 3-(2-Cyanophenyl)-1,5-diphenyl-1,2-dihydropyridin-2-one

[0158] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.32-7.37 (m, 1H), 7.41-7.56 (m, 10H), 7.63 (td, 1H), 7.69 (d, 1H), 7.77-7.82 (m, 2H), 7.98 (d, 1H).
ESI-Mass; 349 [M⁺ + H]

30 Example 42.

3-(2-Cyanophenyl)-5-(2-methoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one

35 [0159] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 3.88 (s, 3H) , 6.95-7.04 (m, 3H) , 7.29-7.54 (m, 7H), 7.58-7.64 (m, 1H), 7.71 (d, 1H), 7.74-7.79 (m, 2H) , 7.95 (d, 1H) .

Example 43.

40 3-(2-Cyanophenyl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0160] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 3.91 (s, 3H), 3.94 (s, 3H), 6.92 (d, 1H) , 7.00-7.02 (m, 1H), 7.04 (dd, 1H) , 7.40-7.59 (m, 6H), 7.60-7.68 (m, 2H) , 7.76-7.79 (m, 1H) , 7.82-7.86 (m, 1H) , 7.97 (d, 1H).

Example 44.

45 3-(2-Cyanophenyl)-5-(thiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0161] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.24 (dd, 1H), 7.35 (dd, 1H), 7.41 (dd, 1H), 7.43-7.56 (m, 6H), 7.63 (dt, 1H), 7.70 (d, 1H), 7.76-7.81 (m, 2H), 7.96 (d, 1H).

50

Example 45.

3-(2-Cyanophenyl)-5-(2-fluorophenyl)-1-phenyl-1,2-dihydropyridin-2-one

55 [0162] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.16 (ddd, 1H), 7.23 (dt, 1H), 7.29-7.36 (m, 1H), 7.42-7.54 (m, 6H), 7.60-7.67 (m, 2H), 7.74-7.81 (m, 3H), 7.92 (dd, 1H).

Example 46.

3-(2-Cyanophenyl)-5-(thiophen-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

5 [0163] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.07 (dd, 1H), 7.17 (dd, 1H), 7.25-7.28 (m, 1H), 7.43-7.56 (m, 6H), 7.64 (dt, 1H), 7.72 (d, 1H), 7.74-7.80 (m, 2H), 7.93 (d, 1H).

Example 47.

10 3-(2-Cyanophenyl)-5-phenyl-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0164] ¹H-NMR (400 MHz, DMSO-d₆); δ (ppm) 7.32-7.39 (1H, m), 7.41-7.47 (2H, m), 7.52-7.65 (2H, m), 7.73-7.80 (4H, m), 7.94 (1H, d), 8.06-8.11 (1H, m), 8.20 (1H, d), 8.25 (1H, d), 8.68 (1H, dd), 8.83 (1H, d).

15 Example 48.

3-(2-Cyanophenyl)-5-(3-furfuryl)-1-(phenyl)-1,2-dihydropyridin-2-one

20 [0165] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 6.55 (dd, 1H), 7.42-7.56 (m, 7H), 7.58 (d, 1H), 7.60-7.67 (m, 2H), 7.74-7.79 (m, 2H), 7.82 (d, 1H).

Example 49.

3-(2-Cyanophenyl)-5-(2-furfuryl)-1-phenyl-1,2-dihydropyridin-2-one

25 [0166] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.12-7.24 (m, 2H), 7.42-7.55 (m, 6H), 7.58-7.65 (m, 3H), 7.66 (d, 1H), 7.74-7.77 (m, 2H).

Example 50.

30 3-(2-Cyanophenyl)-5-(2,4-dimethoxypyrimidin-5-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0167] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 4.03 (s, 3H), 4.07 (s, 3H), 7.42-7.57 (m, 5H), 7.60-7.70 (m, 3H), 7.75-7.80 (m, 2H), 7.86 (d, 1H), 8.29 (s, 1H).

35 Example 51.

3-(2-Cyanophenyl)-5-(3-methoxyridin-5-yl)-1-phenyl-1,2-dihydropyridin-2-one

40 [0168] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 3.92 (s, 3H), 7.30-7.34 (m, 1H), 7.44-7.58 (m, 6H), 7.65 (ddd, 1H), 7.72 (d, 1H), 7.77-7.84 (m, 2H), 7.95 (d, 1H), 8.28-8.33 (m, 1H), 8.36-8.40 (m, 1H).

Example 52.

45 3-(2-Cyanophenyl)-5-(2-methoxyphenyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0169] ¹H-NMR(400MHz, CDCl₃); δ (ppm) 3.89(s,3H), 7.00(d,1H), 7.03-7.08(ddd,1H), 7.35-7.40(m, 2H), 7.46-7.51 (ddd, 1H), 7.63-7.72(m, 2H), 7.72(d, 1H), 7.77-7.80(dd, 1H), 7.82-7.88(m, 1H), 7.95(d, 1H), 8.47-8.52(d, 1H), 8.75-8.80 (m, 1H), 8.96(brs, 1H).

50 Example 53.

3-(2-Cyanophenyl)-5-[2-methoxy-5-(2-cyanophenyl)]-1-(3-pyridyl)-1,2-dihydropyridin-2-one

55 [0170] ¹H-NMR(400MHz, CDCl₃); δ (ppm) 3.97(s, 3H), 7.12(d, 1H), 7.41-7.50(m, 2H), 7.54-7.62(m, 3H), 7.62-7.68 (ddd, 2H), 7.70-7.80(m, 4H) , 8.03(d, 1H) , 8.32-8.38(m, 1H) , 8.71-8.76(m, 1H), 8.93(brs, 1H).

EP 1 300 396 A1

Example 54.

3-(2-Cyanophenyl)-5-(6-methyl-2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0171] ¹H-NMR(400MHz, CDCl₃) ; δ (ppm) 2.56(s, 3H), 7.42-7.70(m, 10H), 7.71-7.78(m, 2H), 7.89-7.93(m, 1H), 8.46-8.54(m, 1H).

[0172] The following compounds were synthesized by the method which is the same as or according to the method mentioned in Example 4.

Example 55.

3-(2-Methoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0173] ¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 3.76 (3H, s) , 7.00 (1H, dt) , 7.09 (1H, d) , 7.25-7.40 (3H, m) , 7.46-7.60 (4H, m) , 7.76-7.84 (2H, m), 7.94 (1H, d), 8.23 (1H, d), 8.38 (1H, d), 8.55-8.58 (1H, m).

Example 56.

3-(2-Methoxyphenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

[0174] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.82 (3H, s), 6.97-7.05 (2H, m), 7.16-7.23 (2H, m), 7.24-7.32 (1H, m), 7.36 (1H, dt), 7.44 (1H, dd), 7.50-7.66 (2H, m), 7.74-7.90 (1H, m) , 8.02-8.08 (1H, m), 8.18-8.45 (2H, m), 8.58-8.64 (1H, m).

Example 57.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0175] ¹H-NMR(CDCl₃, 400MHz) ; δ (ppm) 6.76-6.81(2H,m), 6.86-6.91(1H,m), 7.17-7.22 (2H, m), 7.26-7.75 (5H, m), 7.61 (1H, d), 7.78-7.86 (1H, m), 8.11 (1H, d), 8.41 (1H, brs), 8.60-8.64 (1H, m).

Example 58.

3-(2-Methoxycarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0176] ¹H-NMR (DMSO-d₆, 400 MHz) ; δ (ppm) 3.65 (3H, s), 7.28-7.32 (1H, m), 7.47-7.71 (8H, m), 7.78-7.86 (2H, m), 8.01-8.20 (1H, m), 8.33 (1H, d), 8.42 (1H, d), 8.58-8.60 (1H, m).

Example 59.

3-(2-Methylaminocarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0177] ¹H-NMR (DMSO-d₆, 400MHz) ; δ (ppm) 2.65 (3H, d), 7.26-7.31 (1H, m), 7.40-7.45 (1H, m), 7.46-7.53 (5H, m), 7.53-7.59(2H, m), 7.80-7.86 (1H, m), 7.96 (1H, d), 8.06-8.12 (1H, m), 8.22 (1H, d), 8.37 (1H, d), 8.57-8.60 (1H, m).

Example 60.

3-(2-Tolyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0178] ¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 2.24 (3H, s), 7.22-7.34 (4H, m), 7.47-7.60 (5H, m), 7.78-7.84 (1H, m), 7.99 (1H, d), 8.21-8.24 (1H, m), 8.44-8.47 (1H, m), 8.55-8.59 (1H, m).

Example 61.

3-Phenyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0179] ¹H-NMR (DMSO-d₆, 400 MHz); δ (ppm) 7.28-7.32 (1H, m) , 7.35-7.40 (1H, m), 7.41-7.47 (2H, m), 7.49-7.54 (2H, m), 7.56-7.60 (3H, m), 7.76-7.86 (3H, m), 8.02 (1H, dd), 8.42 (1H, d), 8.44 (1H, d), 8.58-8.61 (1H, m).

Example 62.

3-(2-Pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0180] ¹H-NMR (DMSO-d₆, 400 MHz); δ (ppm) 7.29-7.40 (2H, m), 7.50-7.63 (5H, m), 7.80-7.88 (2H, m), 7.99 (1H, d), 8.50 (1H, d), 8.54 (1H, d), 8.62-8.66 (1H, m), 8.70-8.74 (1H, m), 9.31 (1H, d).

Example 63.

10 3-(3-Cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0181] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.24 (ddd, 1H), 7.46-7.66 (m, 8H), 7.78 (td, 1H), 8.10 (dt, 1H), 8.16 (t, 1H), 8.25 (d, 1H), 8.31 (d, 1H), 8.61-8.63 (m, 1H).

15 Example 64.

3-(4-Cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 20 [0182] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.22-7.26 (m, 1H), 7.47-7.60 (m, 6H), 7.70-7.78 (m, 3H), 7.95-7.98 (m, 2H), 8.26 (d, 1H), 8.33 (d, 1H), 8.61-8.63 (m, 1H).

Example 65.

3-(3-Chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 25 [0183] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.21-7.36 (m, 3H), 7.47-7.76 (m, 5H), 7.58-7.60 (m, 1H), 7.71-7.75 (m, 2H), 7.85 (m, 1H), 8.23-8.26 (m, 2H), 8.60-8.63 (m, 1H).
ESI-Mass; 359 [M⁺ + H]

30 Example 66.

3-(4-Chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 35 [0184] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.22 (ddd, 1H), 7.37-7.41 (m, 2H), 7.44-7.60 (m, 5H), 7.72-7.80 (m, 3H), 8.12-8.16 (m, 1H), 8.21-8.25 (m, 2H), 8.62 (ddd, 1H).
ESI-Mass; 359 [M⁺ + H]

Example 67.

40 3-(3-Pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0185] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.22-7.52 (m, 1H), 7.33-7.37 (m, 1H), 7.45-7.57 (m, 5H), 7.59-7.61 (m, 1H), 7.56 (td, 1H), 8.24-8.27 (m, 2H), 8.30 (d, 1H), 8.59 (dd, 1H), 8.61-8.63 (m, 1H), 8.95-8.96 (m, 1H).
ESI-Mass; 326 [M⁺ + H]

45

Example 68.

3-(2-Aminocarbonyl-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 50 [0186] ¹H-NMR (CDCl₃, 400MHz); δ (ppm) 5.46 (brs, 1H), 7.19 (ddd, 1H), 7.39-7.53 (m, 6H), 7.55-7.58 (m, 1H), 7.58 (brs, 1H), 7.71 (ddd, 1H), 7.82 (dd, 1H), 8.08 (d, 1H), 8.21 (d, 1H), 8.57 (dd, 1H), 8.59 (ddd, 1H).

Example 69.

55 3-(3-Methoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0187] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.84 (s, 3H), 6.92 (ddd, 1H), 7.20 (ddd, 1H), 7.31-7.38 (m, 2H), 7.42-7.55 (m, 6H), 7.57-7.59 (m, 1H), 7.73 (td, 1H), 8.23 (d, 1H), 8.24 (d, 1H), 8.60 (ddd, 1H).

EP 1 300 396 A1

ESI-Mass; 355 [M⁺ + H]

Example 70.

5 3-(4-Methoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2 dihydropyridin-2-one

[0188] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.85 (s, 3H), 6.94-6.98 (m, 2H), 7.20 (ddd, 1H), 7.42-7.55 (m, 5H), 7.57-7.60 (m, 1H), 7.73 (td, 1H), 7.77-7.81 (m, 2H), 8.18-8.20 (m, 2H), 8.59-8.20 (m, 1H). ESI-Mass; 355 [M⁺ + H]

10 Example 71.

3-(2-Fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

15 [0189] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.13-7.22 (m, 3H), 7.31-7.59 (m, 7H), 7.66 (td, 1H), 7.74 (td, 1H), 8.22 (dd, 1H), 8.29(d,1H), 8.58-8.60 (m, 1H).

Example 72.

3-(3-Fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

20 [0190] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.03-7.08 (m, 1H), 7.21 (ddd,1H), 7.35-7.63 (m, 9H), 7.74 (td, 1H), 8.23 (d, 1H), 8.27 (d, 1H), 8.59-8.62 (m, 1H).

Example 73.

25 3-(4-Fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0191] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.08-7.14 (m, 2H), 7.21 (ddd, 1H), 7.44-7.60 (m, 6H), 7.74 (td, 1H), 7.78-7.83 (m, 2H), 8.21 (d, 1H), 8.22(d, 1H) 8.60-8.62 (m, 1H).

30 Example 74.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one

35 [0192] ¹H-NMR (CDCl₃, 400MHz); δ (ppm) 3.84 (s, 3H) , 6.96-7.01 (m, 1H) , 7.04-7.11 (m, 2H), 7.17-7.23 (m, 1H) , 7.26-7.34 (m, 2H), 7.40 (dd, 1H) , 7.46-7.53 (m, 2H) , 7.54-7.58 (m, 1H) , 7.73 (ddd, 1H) , 8.14 (d, 1H), 8.29 (d, 1H), 8.57-8.62 (m, 1H).

Example 75.

40 3-(2,4-Dimethoxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0193] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.93 (s, 6H), 6.93 (d, 1H), 7.19-7.23 (m, 1H), 7.33 (dd, 1H), 7.41-7.57 (m, 6H), 7.58-7.60 (m, 1H), 7.74 (td, 1H), 8.19 (d, 1H), 8.22 (d, 1H), 8.60-8.62 (m, 1H).

45 ESI-Mass; 385 [M⁺ + H]

Example 76.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

50 [0194] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.20-7.28 (m, 2H), 7.44-7.56 (m, 5H), 7.56-7.60 (m, 1H), 7.75 (td, 1H), 8.19-8.21 (m, 1H), 8.26 (ddd, 1H), 8.30 (d, 1H), 8.34 (t, 1H), 8.59-8.61 (m, 1H) ESI-Mass; 344 [M⁺ + H]

Example 77.

55 3-(4-Methoxy-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0195] ¹H-NMR (CDCl₃, 400MHz); δ (ppm) 3.98 (s, 3H) , 6.80 (d, 1H) , 7.22 (ddd, 1H) , 7.44-7.59 (m, 6H) , 7.72-7.77

EP 1 300 396 A1

(m, 1H), 8.15 (dd, 1H), 8.21 (s, 2H), 8.50-8.52 (m, 1H), 8.59-8.62 (m, 1H).
ESI-Mass; 356 [M⁺ + H]

Example 78.

3-(6-Cyano-2-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0196] ¹H-NMR (DMSO-d₆, 400MHz): δ(ppm) 7.30-7.34(ddd, 1H), 7.49-7.57(m, 1H), 7.57-7.62(m, 4H), 7.62-7.66 (dd, 1H), 7.82-7.87(ddd, 1H), 8.02(d, 1H), 8.39-8.43(dd, 1H), 8.59-8.62(m, 1H), 8.63(d, 1H), 8.65(d, 1H), 8.94-8.96 (dd, 1H).

Example 79.

3-(6-Cyano-2-pyridyl)-5-phenyl-1-(3-tyridyl)-1,2-dihydropyridin-2-one

[0197] ¹H-NMR (DMSO-d₆, 400MHz): δ (ppm) 7.33-7.38(m, 1H), 7.44(d, 1H), 7.46(d, 1H), 7.64(d, 1H), 7.65(d, 1H), 7.72-7.76(dd, 2H), 8.07-8.11(m, 1H), 8.30(d, 1H), 8.34(d, 1H), 8.42(dd, 1H), 8.68-8.71(dd, 1H), 8.82-8.84(dd, 1H), 8.93-8.86(dd, 1H).

Example 80.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one

[0198] ¹H-NMR (CDCl₃, 400MHz); δ (ppm) 3.85 (s, 3H), 6.99-7.10 (m, 3H), 7.20-7.31(m,2H), 7.40-7.47(m,1H), 7.58 (d,1H), 7.76(ddd,1H), 8.18-8.23 (m, 1H), 8.23-8.32 (m, 2H), 8.32-8.37 (m, 1H), 8.58-8.64(m,1H).

Example 81.

3-(2-Methoxy-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0199] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 3.98 (s, 3H), 6.96 (dd, 1H), 7.18-7.22 (m, 1H), 7.44-7.59 (m, 6H), 7.74 (dt,1H), 7.90(dd, 1H), 8.17 (dd, 1H), 8.25-8.28 (m, 2H), 8.58-8.61 (m, 1H).

Example 82.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

[0200] ¹H-NMR(CDCl₃,400MHz); δ (ppm) 7.18-7.30 (m,4H), 7.46-7.52(m,2H), 7.58(d, 1H), 7.76 (ddd, 1H), 8.20-8.27 (m, 2H), 8.29 (d, 1H), 8.31-8.35 (m, 1H), 8.59-8.64 (m, 1H).

Example 83.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-1,2-dihydropyridin-2-one

[0201] ¹H-NMR(CDCl₃, 400 MHz) ; δ (ppm) 7.25-7.32 (m, 2H), 7.61 (d, 1H), 7.79(ddd,1H), 8.16-8.22(m, 1H), 8.24-8.27(m,1H), 8.29(d,1H), 8.34-8.37 (m, 1H), 8.61-8.64 (m, 1H), 9.01 (s, 2H), 9.32(s, 1H).

Example 84.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one

[0202] ¹H-NMR(CDCl₃, 400 MHz) ; δ (ppm) 2.53 (s, 3H), 7.20-7.28 (m, 2H), 7.36-7.43 (m, 4H), 7.57 (d, 1H), 7.75 (td, 1H), 8.19-8.27 (m, 2H), 8.28 (d, 1H), 8.33 (t, 1H), 8.59-8.61(m, 1H).
ESI-Mass; 390 [M⁺ + H]

EP 1 300 396 A1

Example 85.

3-(2-Pyridon-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0203] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 6.67 (d, 1H), 7.21-7.26 (m, 1H), 7.45-7.59 (m, 6H), 7.75 (td, 1H), 7.96 (dd, 1H), 8.14 (d, 1H), 8.26 (d, 1H), 8.32 (m, 1H), 8.62 (m, 1H).
ESI-Mass; 342 [M⁺ + H]

Example 86.

10

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(4-methoxy-3-pyridyl)-1,2-dihydropyridin-2-one

[0204] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 4.00 (s, 3H), 6.88 (dd, 1H), 7.22-7.29 (m, 2H), 7.44-7.79 (m, 5H), 8.20-8.24(m, 1H), 8.27-8.29(m, 1H), 8.33-8.36(m,1H), 8.61(ddd, 1H).

15

Example 87.

3-(2-Fluoro-3-pyridyl)-5-phenyl-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- 20 [0205] ¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 7.31-7.37(m, 1H), 7.41-7.48(m, 2H), 7.52-7.66(m, 2H), 7.71-7.76(d, 2H), 8.06-8.10(m, 1H), 8.16-8.28(m, 4H), 8.66-8.70(dd, 1H), 8.80-8.82(d, 1H).

Example 88.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one

- 25 [0206] ¹H-NMR (CDCl₃, 400 MHz); δ (ppm) 7.17-7.33 (m, 5H), 7.48-7.55 (m, 1H), 7.56-7.61 (m, 1H), 7.76 (ddd, 1H), 8.20-8.27 (m, 2H), 8.29 (d, 1H), 8.32-8.35 (m, 1H), 8.59-8.63 (m, 1H).

30 Example 89.

3-(2-Dimethylamino-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 35 [0207] ¹H-NMR (CDCl₃, 400MHz); δ (ppm) 1.70(s, 6H), 7.19(ddd, 1H), 7.41-7.60(m, 7H), 7.71(td, 1H), 7.82(d, 1H), 8.08(d, 1H), 8.21(d, 1H), 8.57(dd, 1H), 8.58-8.60(m, 1H).
ESI-Mass; 369 [M⁺ + H]
[0208] The following compounds were synthesized by the same method as mentioned in Example 7.

Example 90.

40

3,5-Diphenyl-1-(2-pyridyl)-1,2-dihydropyridin-2-one

[0209] ¹H-NMR(400MHz, CDCl₃) ; δ (ppm) 7.33-7.40(3H,m), 7.41-7.47(4H,m), 7.54(2H, dd), 7.76(2H, dd), 7.86-7.90 (2H, m), 7.99 (1H, ddd), 8.11 (1H, d), 8.61-8.64 (1H, m).

45

Example 91.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

- 50 [0210] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.18-7.25 (m, 3H), 7.44-7.55 (m, 3H), 7.59-7.67 (m, 2H), 7.72-7.81 (m, 3H), 8.27-8.33 (m, 2H), 8.58-8.63 (m, 1H).

Example 92.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one

[0211] ¹H-NMR (400 MHz, CDCl₃); δ (ppm) 7.15-7.25 (m, 2H), 7.28-7.36 (m, 2H), 7.44-7.54 (m, 2H), 7.58-7.68 (m, 2H), 7.72-7.82 (m, 3H), 8.28-8.33 (m, 2H), 8.57-8.63 (m, 1H).

EP 1 300 396 A1

Example 93.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-cyanophenyl)-1,2-dihydropyridin-2-one

5 [0212] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.23-7.26(m, 1H), 7.49 (dt, 1H), 7.61-7.86 (m, 9H), 7.28-8.30 (m, 2H), 8.60-8.62 (m, 1H).

Example 94.

10 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-cyanophenyl)-1,2 dihydropyridin-2-one

[0213] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.23-7.26 (m, 1H), 7.49 (dt, 1H), 7.61-7.89 (m, 9H), 8.30 (s, 2H), 8.60-8.62 (m, 1H).

15 Example 95.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one

20 [0214] ¹H-NMR(400MHz, CDCl₃) ; δ(ppm)3.86 (s,3H), 7.02(d,2H), 7.21(ddd,1H), 7.42-7.80(m,8H), 8.29(d,1H), 8.31 (d,1H), 8.58-8.60(m,1H).

Example 96.

25 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one

[0215] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 3.85 (s, 3H), 6.95-7.03 (m, 1H), 7.06-7.10(m,2H), 7.20-7.22(m,1H), 7.41-7.81(m,7H), 8.31(s,2H), 8.59-8.61 (m, 1H).

Example 97.

30 3-Phenyl-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one

[0216] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.15-7.24 (m, 2H), 7.26-7.33 (m, 2H), 7.34-7.40 (m, 1H), 7.40-7.53 (m, 3H), 7.57-7.62(m, 1H), 7.72-7.82 (m, 3H), 8.20-8.23 (m, 2H), 8.59-8.63 (m, 1H).

35

Example 98.

3-Phenyl-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

40 [0217] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.18-7.24 (m, 3H), 7.34-7.39 (m, 1H), 7.40-7.45 (m, 2H), 7.46-7.52 (m, 2H), 7.57-7.61 (m, 1H), 7.72-7.77 (m, 1H), 7.77-7.82 (m, 2H), 8.19-8.23 (m, 2H), 8.59-8.62 (m, 1H).

Example 99.

45 3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

[0218] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.16-7.24 (m, 3H), 7.29-7.35 (m, 2H), 7.45-7.54(m,4H), 7.56(d,1H), 7.70-7.76(m,1H), 8.12 (d,1H), 8.28 (d, 1H), 8.58-8.62 (m, 1H).

50 Example 100.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-formylphenyl)-1,2-dihydropyridin-2-one

55 [0219] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.22-7.27 (m, 1H), 7.48 (ddd, 1H), 7.60-7.69 (m, 2H), 7.72-7.82 (m, 5H), 8.03-8.09 (m, 2H), 8.29 (d, 1H), 8.33 (d, 1H), 8.58-8.62 (m, 1H), 10.10 (s, 1H).

EP 1 300 396 A1

Example 101.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-formylphenyl)-1,2-dihydropyridin-2-one

5 [0220] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.20-7.25 (m, 1H), 7.44-7.52 (m, 2H), 7.61-7.70 (m, 3H), 7.73-7.83 (m, 4H), 8.06 (dd, 1H), 8.31 (d, 1H), 8.36 (d, 1H), 8.57-8.60 (m, 1H), 10.05 (s, 1H).

Example 102.

10 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-chlorophenyl)-1,2-dihydropyridin-2-one

[0221] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.21-7.25 (m, 1H), 7.43-7.50 (m, 4H), 7.55-7.58 (m, 1H), 7.59-7.68 (m, 2H), 7.73-7.81 (m, 3H), 8.27-8.31 (m, 2H), 8.58-8.62 (m, 1H).

15 Example 103.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-tolyl)-1,2-dihydropyridin-2-one

20 [0222] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 2.43 (s, 3H), 7.20-7.23 (m, 1H), 7.26-7.35 (m, 3H), 7.39-7.48 (m, 2H), 7.60-7.66 (m, 2H), 7.72-7.81 (m, 3H), 8.31 (s, 2H), 8.58-8.61 (m, 1H).

Example 104.

25 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-trifluoromethylphenyl)-1,2-dihydropyridin-2-one

[0223] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.22-7.25 (m, 1H), 7.47 (t, 1H), 7.61-7.82 (m, 9H), 8.31 (s, 2H), 8.59-8.62 (m, 1H).

Example 105.

30 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(thiophen-3-yl)-1,2-dihydropyridin-2-one

[0224] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.22-7.25 (m, 1H), 7.37-7.49 (m, 3H), 7.59-7.67 (m, 3H), 7.74-7.80 (m, 3H), 8.27 (d, 1H), 8.40 (d, 1H), 8.60-8.62 (m, 1H).

35

Example 106.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-furfuryl)-1,2-dihydropyridin-2-one

40 [0225] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 6.83-6.86 (m, 1H), 7.19-7.26 (m, 1H), 7.48 (ddd, 1H), 7.52 (dd, 1H), 7.60-7.69 (m, 2H), 7.73-7.82 (m, 3H), 8.21 (d, 1H), 8.27-8.30 (m, 1H), 8.47 (d, 1H), 8.61-8.65 (m, 1H).

Example 107.

45 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-tolyl)-1,2-dihydropyridin-2-one

[0226] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 2.41 (s, 3H), 7.18-7.22 (m, 1H), 7.30-7.46 (m, 5H), 7.59-7.65 (m, 2H), 7.71-7.80 (m, 3H), 8.29 (d, 1H), 8.31 (d, 1H), 8.58-8.60 (m, 1H).

50 Example 108.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-trifluoromethylphenyl)-1,2-dihydropyridin-2-one

55 [0227] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.22-7.25 (m, 1H), 7.48 (td, 1H), 7.61-7.82 (m, 9H), 8.30 (d, 1H), 8.32 (d, 1H), 8.59-8.61 (m, 1H).

EP 1 300 396 A1

Example 109.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-methoxypyridin-5-yl)-1,2-dihydropyridin-2-one

5 [0228] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 4.00 (s, 3H), 6.88 (d, 1H), 7.23 (ddd, 1H), 7.47 (td, 1H), 7.59-7.62 (m, 1H), 7.65 (td, 1H), 7.73-7.82 (m, 4H), 8.28-8.31 (m, 3H), 8.60 (ddd, 1H).
ESI-Mass; 381 [M⁺ + H]

Example 110.

10

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-cyanophenyl)-1,2-dihydropyridin-2-one

[0229] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.26-7.35 (m, 2H), 7.52-7.58 (m, 2H), 7.64-7.71 (m, 2H), 7.72-7.85 (m, 5H), 8.51 (d, 1H), 8.68-8.72 (m, 1H), 8.77 (d, 1H).

15

Example 111.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-1,2-dihydropyridin-2-one

20 [0230] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.24-7.32 (m, 1H), 7.48-7.54 (m, 1H), 7.61-7.72 (m, 2H), 7.73-7.85 (m, 3H), 8.31 (d, 1H), 8.33 (d, 1H), 8.60-8.65 (m, 1H), 9.04 (s, 2H), 9.32 (s, 1H).

Example 112.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[2-(pyrrolidin-1-yl)-pyridin-5-yl]-1,2-dihydropyridin-2-one

[0231] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 2.01-2.07 (m, 4H), 3.49-3.52 (m, 4H), 6.44 (dd, 1H), 7.21 (ddd, 1H), 7.45 (td, 1H), 7.58-7.67 (m, 3H), 7.72 (dd, 1H), 7.76-7.88 (m, 2H), 8.23 (dd, 1H), 8.28 (dd, 2H), 8.59 (ddd, 1H).
ESI-Mass; 420 [M⁺ + H]

30

Example 113.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[2-(4-benzylpiperazin-1-yl)-pyridin-5-yl]-1,2-dihydropyridin-2-one

35 [0232] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 2.57 (t, 4H), 3.63 (t, 4H), 3.57 (s, 2H), 6.70 (d, 1H), 7.21 (ddd, 1H), 7.25-7.38 (m, 5H), 7.45 (td, 1H), 7.58 (d, 1H), 7.63 (td, 1H), 7.68 (dd, 1H), 7.73 (dd, 1H), 7.75-7.79 (m, 2H), 8.26-8.29 (m, 3H), 8.58-8.60 (m, 1H).

Example 114.

40

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-benzyloxyethoxypyridin-5-yl)-1,2-dihydropyridin-2-one

[0233] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 3.84-3.87 (m, 2H), 4.55-4.58 (m, 2H), 4.64 (s, 2H), 6.93 (d, 1H), 7.23 (ddd, 1H), 7.25-7.40 (m, 5H), 7.47 (td, 1H), 7.60 (d, 1H), 7.65 (td, 1H), 7.74-7.82 (m, 4H), 8.27 (d, 1H), 8.28 (d, 1H), 8.30 (d, 1H), 8.59-8.61 (m, 1H). ESI-Mass; 501 [M⁺ + H]

45

Example 115.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-benzyloxymethylpyridin-5-yl)-1,2-dihydropyridin-2-one

50

[0234] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 4.64 (s, 2H), 4.66 (s, 2H), 7.23-7.26 (m, 1H), 7.26-7.38 (m, 5H), 7.48 (td, 1H), 7.61 (d, 1H), 7.68 (td, 1H), 7.74-7.81 (m, 3H), 7.95-7.98 (m, 1H), 8.29 (d, 1H), 8.32 (d, 1H), 8.61 (d, 1H), 8.69 (d, 1H), 8.72 (d, 1H).
ESI-Mass; 471 [M⁺ + H]

55

EP 1 300 396 A1

Example 116.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-ethylthiopyridin-5-yl)-1,2-dihydropyridin-2-one

5 [0235] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 1.41 (t, 3H), 3.23 (q, 2H), 7.23 (ddd, 1H), 7.29 (dd, 1H), 7.47 (td, 1H), 7.60 (dt, 1H), 7.65 (td, 1H), 7.72 (dd, 1H), 7.74-7.80 (m, 3H), 8.28 (d, 1H), 8.30 (d, 1H), 8.57 (dd, 1H), 8.60 (ddd, 1H).

Example 117.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-pyridyl)-1,2-dihydropyridin-2-one

10 [0236] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.23-7.26 (m, 1H), 7.49 (td, 1H), 7.55-7.57 (m, 2H), 7.61 (d, 1H), 7.67 (td, 1H), 7.73-7.81 (m, 3H), 8.29 (d, 1H), 8.30 (d, 1H), 8.61 (ddd, 1H), 8.82 (d, 2H).
ESI-Mass; 351 [M⁺ + H]

Example 118.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-methoxypyridin-5-yl)-1,2-dihydropyridin-2-one

20 [0237] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 3.91 (s, 3H), 7.22-7.27 (m, 1H), 7.46-7.51 (m, 2H), 7.60-7.64 (m, 1H), 7.66 (ddd, 1H), 7.74-7.82 (m, 3H), 8.30 (d, 1H), 8.32 (d, 1H), 8.38 (d, 1H), 8.43 (d, 1H), 8.60-8.63 (m, 1H).

Example 119.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxyethoxypyridin-5-yl)-1,2-dihydropyridin-2-one

25 [0238] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 3.04 (brs, 1H), 3.97-4.03 (m, 2H), 4.51-4.54 (m, 2H), 6.93 (d, 1H), 7.23 (dd, 1H), 7.47 (td, 1H), 7.61 (dd, 1H), 7.65 (td, 1H), 7.74-7.80 (m, 3H), 7.84 (dd, 1H), 8.27-8.30 (m, 3H), 8.61 (ddd, 1H).
ESI-Mass; 411 [M⁺ + H]

Example 120.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-chloropyridin-5-yl)-1,2-dihydropyridin-2-one

35 [0239] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.23-7.28 (m, 1H), 7.47-7.52 (m, 2H), 7.61 (d, 1H), 7.67 (t, 1H), 7.72-7.81 (m, 3H), 7.95 (dd, 1H), 8.28 (d, 1H), 8.30 (d, 1H), 8.59 (d, 1H), 8.61 (dt, 1H). ESI-Mass; 385 [M + H]

Example 121.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-[2-(4-methylpiperazin-1-yl)-pyridin-5-yl]-1,2-dihydropyridin-2-one

40 [0240] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 2.37 (s, 3H), 2.54 (t, 4H), 3.66 (t, 4H), 6.73 (d, 1H), 7.21 (ddd, 1H), 7.46 (td, 1H), 7.59 (d, 1H), 7.64 (td, 1H), 7.70 (dd, 1H), 7.72-7.79 (m, 3H), 8.27-8.29 (m, 3H), 8.58-8.60 (m, 1H).
ESI-Mass; 449 [M⁺ + H]

Example 122.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(3-tert-butyl dimethylsilyloxymethylpyridin-5-yl)-1,2-dihydropyridin-2-one

50 [0241] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 0.13 (s, 6H), 0.95 (s, 9H), 4.85 (s, 2H), 7.24 (dd, 1H), 7.45-7.81 (m, 7H), 7.88 (s, 1H), 8.29 (d, 1H), 8.32 (d, 1H), 8.61 (dd, 1H), 8.68 (d, 1H).

Example 123.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-fluoronyridin-5-yl)-1,2-dihydropyridin-2-one

55 [0242] ¹H-NMR (400 MHz, CDCl₃) ; δ (ppm) 7.11 (dd, 1H), 7.25 (ddd, 1H), 7.42-7.84 (m, 6H), 8.08 (ddd, 1H), 8.30 (t, 2H), 8.41 (dd, 1H), 8.61 (ddd, 1H).

EP 1 300 396 A1

ESI-Mass; 369 [M⁺ + H]

Example 124.

5 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-ethylpyridine-5-yl)-1,2-dihydropyridin-2-one

[0243] ¹H-NMR(400MHz, CDCl₃) ; δ (ppm) 1.36(t,3H), 2.91(q,2H), 7.23(m,1H), 7.33(d,1H), 7.47(td,1H), 7.60(d,1H), 7.65(td,1H), 7.73-7.80(m,3H), 7.86(dd,1H), 8.30(d,1H), 8.31(d, 1H), 8.60(d,1H), 8.68(d,1H).

ESI-Mass; 379 [M⁺ + H]

10

Example 125.

3-Phenyl-5-(2-pyridyl)-1-(2-cyanophenyl)-1,2-dihydropyridin-2-one

15 [0244] ¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 7.24-7.54(6H,m), 7.62-7.81(4H,m), 7.93(1H, dt), 8.11(1H,d), 8.57(1H, d), 8.69-8.72(1H,m), 8.89-8.94(1H,m).

Example 126.

20 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-methoxyphenyl)-1,2-dihydropyridin-2-one

[0245] ¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 3.80(3H,s), 7.12(1H,t), 7.24-7.33(2H,m), 7.44(1H,dd), 7.49(1H,dt), 7.59(1H,dt), 7.71(1H,d), 7.75-7.86(2H,m), 7.90-8.00(2H,m), 8.42(1H,d), 8.47(1H,d), 8.56-8.60(1H,m).

[0246] The following compounds were synthesized by the same method as mentioned in Example 32.

25

Example 127.

3-Phenyl-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

30 [0247] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23(ddd,1H), 7.36-7.50(m,4H), 7.60(td,1H), 7.75(dd,1H), 7.76-7.80(m, 2H), 7.94(ddd,1H), 8.22(d,1H), 8.24(d,1H), 8.62(ddd,1H), 8.71(dd,1H), 8.75-8.79(m, 1H).

ESI-Mass; 326 [M⁺ + H]

Example 128.

35

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0248] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23(ddd,1H), 7.31-7.36(m,2H), 7.41-7.51(m,3H), 7.56-7.59(m,1H), 7.75 (td,1H), 7.95(ddd,1H), 8.15(d,1H), 8.30(d,1H), 8.60-8.62(m,1H), 8.69(dd,1H), 8.80(d,1H).

40

ESI-Mass; 360 [M⁺ + H]

Example 129.

3-(2-Methoxyphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

45

[0249] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.84(s,3H), 6.98-7.05(m,2H), 7.21(ddd,1H), 7.37(td,1H), 7.41-7.49(m, 2H), 7.56(d,1H), 7.74(td,1H), 7.94-7.97(m,1H), 8.13(d,1H), 8.25(d,1H), 8.58-8.60(m,1H), 8.67(dd,1H), 8.79(d,1H).

ESI-Mass; 356 [M⁺ + H]

50

Example 130.

3-(2-Formylthiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

55

[0250] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.24-7.28(m,1H), 7.46-7.52(m,2H), 7.57(d,1H), 7.50-7.79(m,2H), 7.92-7.96(m,1H), 8.24(d,1H), 8.30(d,1H), 8.61-8.63(m,1H), 8.74(dd,1H), 8.79(d,1H), 9.99(d,1H).

EP 1 300 396 A1

Example 131.

3-(2,4-Dichlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- 5 [0251] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.22-7.25(m,1H), 7.32(dd,1H), 7.41-7.61(m,4H), 7.74-7.79(m,1H), 7.93-7.96(m,1H), 8.15(d,1H), 8.29(d,1H), 8.59-8.63(m,1H), 8.69-8.72(m,1H), 8.79(d,1H).
ESI-Mass; 394 [M⁺ + H]

Example 132.

10

3-(2-Trifluoromethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- [0252] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.22(ddd,1H), 7.44-7.56(m,4H), 7.59-7.63(m,2H), 7.72-7.78(m,1H), 7.94(ddd,1H), 8.04(d,1H), 8.30(d,1H), 8.59-8.61(m,1H), 8.69(dd,1H), 8.78-8.79(m,1H).
15 ESI-Mass; 394 [M⁺ + H]

Example 133.

3-(Thiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

20

- [0253] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.24(ddd,1H), 7.39(dd,1H), 7.50(dd,1H), 7.60-7.63(m,1H), 7.65(dd,1H), 7.77(td,1H), 7.93(ddd,1H), 8.15(d,1H), 8.32(dd,1H), 8.44(d,1H), 8.62-8.64(m,1H), 8.72-8.73(m,1H), 8.77(d,1H).
ESI-Mass; 332 [M⁺ + H]

25

Example 134.

3-(1-tert-Butoxycarbonylpyrrol-2-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- [0254] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.47(s,9H), 6.25(t,1H), 6.36-6.34(m,1H), 7.21(dd,1H), 7.37(dd,1H),
30 7.43-7.48(m,1H), 7.57(d,1H), 7.72-7.77(m,1H), 7.88-7.92(m,1H), 8.06(d,1H), 8.22(d,1H), 8.59-8.61(m,1H), 8.68(dd,1H), 8.76(d,1H).
ESI-Mass; 415 [M⁺ + H]

Example 135.

35

3-(2,6-Dimethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- [0255] ¹H-NMR(400MHz, CDCl₃); δ (ppm) 2.23(s,6H), 7.11-7.27(m,3H), 7.45-7.55(m,3H), 7.65-8.02(m,2H),
40 8.20-8.33(m,1H), 8.59-8.61(m,1H), 8.68-8.81(m,3H).
ESI-Mass; 354 [M⁺ + H]

Example 136.

3-(3-Acetylaminophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

45

- [0256] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.08(s,3H), 7.21-7.26(m,1H), 7.34(d,1H), 7.44-7.49(m,2H), 7.58-7.61(m,2H), 7.75(td,1H), 7.82(bris,1H), 7.86(m,1H), 7.89-7.92(m,1H), 8.20-8.23(m,2H), 8.59-8.61(m,1H), 8.69-8.71(m,1H),
50 8.77-8.78(m,1H).
ESI-Mass; 383 [M⁺ + H]

Example 137.

3-(2-Cyanothiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- 55 [0257] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23-7.26(m,1H), 7.50(dd,1H), 7.61-7.74(m,3H), 7.79(td,1H), 7.91-7.94(m,1H), 8.36(d,1H), 8.57(d,1H), 8.60-8.61(m,1H), 8.74(dd,1H), 8.79(d,1H).
ESI-Mass; 357 [M⁺ + H]

Example 138.

3-(2-Cyano-6-methoxyphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- 5 [0258] ¹H-NMR (400MHz, CDCl₃): δ (ppm) 3.82(s,3H), 7.18-7.27(m,2H), 7.35-7.38(dd,1H), 7.43-7.50(m,2H), 7.60(d,1H), 7.74-7.80(ddd,1H), 7.98-8.02(m,1H), 8.16(d,1H), 8.35(d,1H), 8.59-8.62(m,1H), 8.67-8.72(dd,1H), 8.83(d,1H).

Example 139.

10 3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0259] ¹H-NMR (400MHz, CDCl₃): δ (ppm) 7.21-7.29(m,2H), 7.45-7.52(m,1H), 7.59(d,1H), 7.78(dt,1H), 7.91-7.95(m,1H), 8.19-8.25(m,2H), 8.30(d,1H), 8.35(t,1H), 8.60-8.63(m,1H), 8.70-8.73(m,1H), 8.79(d,1H).

[0260] The following compound was synthesized by the same method as mentioned in Example 15.

15

Example 140.

3-(2-Aminocarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 20 [0261] ¹H-NMR (DMSO-d₆, 400MHz): δ (ppm) 7.17(1H,brs), 7.26-7.31(1H,m), 7.40-7.64(10H,m), 7.82(1H,dt), 7.96(1H,d), 8.21(1H,d), 8.36(1H,d), 8.56-8.59(1H,m).

[0262] The following compounds were synthesized by the same method as mentioned in Example 18.

Example 141.

25

3-(2-Hydroxyphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0263] ¹H-NMR (DMSO-d₆, 400MHz): δ (ppm) 6.87-6.93(2H,m), 7.22(1H,dt), 7.30(1H,ddd), 7.38(1H,dd), 7.48-7.60(5H,m), 7.82(1H,dt), 7.99(1H,d), 8.41(1H,d), 8.45(1H,d), 8.57-8.60(1H,m), 9.43(1H,s).

30

Example 142.

3-(2-Hydroxyphenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one

- 35 [0264] ¹H-NMR (DMSO-d₆, 400MHz): δ (ppm) 6.86-6.93(2H,m), 7.22(1H,dt), 7.30(1H,ddd), 7.36-7.44(3H,m), 7.62-7.68(2H,m), 7.83(1H,dt), 7.98(1H,d), 8.40(1H,d), 8.45(1H,d), 8.57-8.60(1H,m), 9.40(1H,s).

Example 143.

40 3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one

[0265] ¹H-NMR (400MHz, CDCl₃): δ (ppm) 6.71-6.76(m,1H), 6.85-6.91(m,2H), 7.19-7.34(m,4H), 7.41-7.50(m,2H), 7.56(d,1H), 7.74(ddd,1H), 8.17(d,1H), 8.23(d,1H), 8.58-8.62(m,1H).

[0266] The following compounds were synthesized by the same method as mentioned in Example 19.

45

Example 144.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one

- 50 [0267] ¹H-NMR (400MHz, CDCl₃): δ (ppm) 2.89(s,6H), 3.41(t,2H), 4.54(t,2H), 6.99-7.04(m,1H), 7.13(dd,1H), 7.14-7.18(m,1H), 7.21(ddd,1H), 7.30-7.35(m,2H), 7.43-7.51(m,3H), 7.58(d,1H), 7.74(ddd,1H), 8.15(d,1H), 8.28(d,1H), 8.59-8.62(m,1H).

Example 145.

55

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(4-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one

[0268] ¹H-NMR (400MHz, CDCl₃): δ (ppm) 1.98(tt,2H), 2.26(s,6H), 2.46(t,2H), 4.06(t,2H), 6.97-7.03(m,2H), 7.19

EP 1 300 396 A1

(ddd,1H), 7.28-7.33(m,2H), 7.39-7.44(m,2H), 7.46-7.51(m,2H), 7.53-7.58(m,1H), 7.72(ddd,1H), 8.12(d,1H), 8.28(d,1H), 8.58-8.61(m,1H).

Example 146.

3-(2-Chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one

[0269] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.96(tt,2H), 2.25(s,6H), 2.44(t,2H), 4.05(t,2H), 6.95-7.01(m,1H), 7.04-7.11(m,2H), 7.17-7.24(m,1H), 7.28-7.35(m,2H), 7.36-7.43(m,1H), 7.45-7.53(m,2H), 7.56(d,1H), 7.73(ddd,1H), 8.14(d,1H), 8.29(d,1H), 8.58-8.63(m,1H).

[0270] The following compounds were synthesized by the same method as mentioned in Example 21.

Example 147.

3-(2-Hydroxymethylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0271] ¹H-NMR (DMSO-d₆; 400MHz); δ (ppm) 4.46(2H,d), 5.04(1H,t), 7.24-7.60(10H,m), 7.78-7.84(1H,m), 7.96-8.00(1H,m), 8.25(1H,d), 8.45(1H,d), 8.55-8.59(1H,m).

Example 148.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-hydroxymethylphenyl)-1,2-dihydropyridin-2-one

[0272] ¹H-NMR(400MHz, CDCl₃); δ (ppm) 1.81(t,1H), 4.78(d,2H), 7.19-7.24(m,1H), 7.46(ddd,1H), 7.51-7.55(m,4H), 7.59-7.66(m,2H), 7.72-7.80(m,3H), 8.28-8.32(m,2H), 8.58-8.61(m,1H).

Example 149.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxymethylphenyl)-1,2-dihydropyridin-2-one

[0273] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.35(dd,1H), 4.52(dd,1H), 4.62(dd,1H), 7.21-7.24 (m,1H), 7.35(dd,1H), 7.46-7.57(m,3H), 7.60-7.69(m,3H), 7.72-7.81(m,3H), 8.26(d,1H), 8.36(d,1H), 8.58-8.62(m,1H).

[0274] The following compounds were synthesized by the same method as mentioned in Example 22.

Example 150.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4-cyanomethylphenyl)-1,2-dihydropyridin-2-one

[0275] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.84(s,2H), 7.23(ddd,1H), 7.47(ddd,1H), 7.49-7.54(m,2H), 7.55-7.63(m,3H), 7.65(ddd,1H), 7.73-7.81(m,3H), 8.28-8.32(m,2H), 8.58-8.62(m,1H).

Example 151.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-cyanomethylphenyl)-1,2-dihydropyridin-2-one

[0276] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 3.81(d,1H), 3.91(d,1H), 7.24(ddd,1H), 7.39-7.44(m,1H), 7.46-7.58(m,3H), 7.62(d,1H), 7.64-7.71(m,3H), 7.73-7.81(m,2H), 8.22(d,1H), 8.34(d,1H), 8.59-8.63(m,1H).

[0277] The following compounds were synthesized by the same method as mentioned in Example 27.

Example 152.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-ethylsulfonylpyridin-5-yl)-1,2-dihydropyridin-2-one

[0278] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.36(t,3H), 3.47(q,2H), 7.26-7.29(m,1H), 7.51(td,1H), 7.63(d,1H), 7.68(td,1H), 7.71-7.82(m,3H), 8.23-8.29(m,2H), 8.31-8.33(m,2H), 8.61-8.63(m,1H), 8.97-8.98(m,1H).

ESI-Mass; 443 [M⁺ + H]

EP 1 300 396 A1

Example 153.

3-(2-Fluoro-3-pyridyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one

5 [0279] ¹H-NMR (400MHz, CDCl₃) ; δ (ppm) 3.11(s,3H), 7.24-7.30(m,2H), 7.60(d,1H), 7.75-7.80(m,3H), 8.12(t,1H), 8.14(t,1H), 8.17-8.24(m,2H), 8.30(d,1H), 8.35(t,1H), 8.61-8.63(m,1H). ESI-Mass; 422 [M⁺ + H]

[0280] The following compounds were synthesized by the same manner as mentioned in Example 29.

Example 154.

10

3-(2-Dimethylaminomethylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one dihydrochloride

[0281] ¹H-NMR (DMSO-d₆, 400MHz); δ (ppm) 2.06(6H,s), 3.37(2H,s), 7.25-7.39(4H,m), 7.44-7.61(6H,m), 7.81(1H, dt) 7.96(1H,d) 8.24(1H,d), 8.43(1H,d), 8.55-8.58(1H,m).

15

Example 155.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-dimethylaminomethylphenyl)-1,2-dihydropyridin-2-one

20 [0282] ¹H-NMR (400MHz, CDCl₃) ; δ (ppm) 2.16(s,6H) 3.30(d, 1H), 3.46(d,1H), 7.18-7.23(m,1H), 7.34-7.38(m,1H), 7.40-7.49(m,3H), 7.55-7.66(m,3H), 7.70-7.79(m,3H), 8.21(d, 1H), 8.37(d,1H), 8.58-8.61(m,1H).

Example 156.

25

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(4 dimethylaminomethylphenyl)-1,2-dihydropyridin-2-one

[0283] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 2.28(s,6H), 3.49(s,2H), 7.22(ddd,1H), 7.43-7.49(m,5H), 7.59-7.66(m,2H), 7.72-7.81(m,3H), 8.30(d,1H), 8.33(d,1H) 8.58-8.61(m,1H).

30

Example 157.

3-(2-Cyanophenyl)-5-(6-diethylaminomethyl-2-pyridyl)-1-phenyl-1,2-dihydroDyridin-2-one

35 [0284] ¹H-NMR (400MHz, CDCl₃); δ (ppm) 1.49(6H,t), 3.10-3.33(4H,m), 4.36(2H,brs), 7.46-7.60(7H,m), 7.63-7.68 (2H,m), 7.79-7.89(3H,m), 8.28(1H,d), 8.39(1H,d).

[0285] The following compound was synthesized by the same method as mentioned in Example 31.

Example 158.

40

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-phenethyl-1,2-dihydropyridin-2-one

[0286] ¹H-NMR (400MHz, CDCl₃) ; δ (ppm) 3.18(t,2H), 4.33(t,2H), 7.19(ddd,1H), 7.22-7.34(m,3H), 7.39(d,1H), 7.43-7.50(m,3H), 7.62-7.74(m,4H), 7.96(d,1H), 8.18(d,1H), 8.56-8.60(m,1H).

45

Example 159.

3-(2-Cyanophenyl)-1-(2-pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

50

[0287] A mixture of 0.05g of 1-(2-pyridyl)-5-(2-pyridyl)-3-bromo-1,2-dihydropyridin-2-one, 0.04g of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 0.02g of tetrakis(triphenylphosphine) palladium and 0.1g of cesium carbonate was stirred at 120°C in a nitrogen atmosphere for 2 hours in dimethylformamide. The mixture was diluted with water, and extracted with ethyl acetate. The organic layer was washed with water and then saturated saline water, and dried by magnesium sulfate anhydride. The solvent was concentrated under a vacuum, and the residue was refined by silica gel chromatography (ethyl acetate/hexane=3:1), to obtain 0.04g of the white, powdery subject compound.

55

¹H-NMR (400MHz, DMSO-d₆) ; δ (ppm) 7.33(dd, 1H), 7.56-7.64(m, 2H), 7.75(d, 1H), 7.78-7.83(m, 1H), 7.84-7.90(m, 2H), 7.95(d, 1H), 8.00(d,1H), 8.07(dt, 1H), 8.50(d, 1H), 8.61(d, 1H), 8.70(d, 1H), 8.83(d, 1H).

Example 160.

1-(2-Cyanophenyl)-3-(2-pyridyl)-5-phenyl-1,2-dihydropyridin-2-one

- 5 [0288] 5ml of a dimethylformamide solution containing 0.26g of 3-(2-pyridyl)-5-phenyl-2(1H)-pyridone was incorporated with 0.04g of sodium hydride. After 15 minutes, the solution was further incorporated with 0.15g of 2-fluorobenzonitrile and 0.10g of cuprous iodide, and vigorously stirred at 100°C for 2 hours. The solution was cooled to room temperature, diluted with water, and extracted with ethyl acetate. The organic layer was washed with water and then saturated saline water, and dried by magnesium sulfate anhydride. The solvent was distilled off under a vacuum. The residue was refined by silica gel chromatography (ethyl acetate/hexane=1:2), to obtain 0.03g of the light yellow, powdery subject compound.

¹H-NMR (400MHz, DMSO-d₆) ; δ(ppm) 7.34-7.42(m,2H), 7.45-7.50(m,2H), 7.70-7.78(m, 3H), 7.84-7.90(m, 2H), 7.96(dt, 1H), 8.11(d, 1H), 8.31(d, 1H), 8.47(dd, 1H), 8.71-8.74(m, 1H), 8.88(d, 1H).

15 Example 161.

1-Phenyl-3-(1-phenylacetylen-2-yl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 20 [0289] 100mg of 3-bromo-1-phenyl-5-(pyridin-2-yl)-1,2-dihydropyridin-2-one, 55mg of phenylacetylene, 1mg of copper (I) iodide and 4mg of dichlorobis(triphenylphosphine) palladium were added to a mixed solvent of 1.5ml of triethylamine and 1ml of dimethylformamide, and stirred at 50°C in a nitrogen atmosphere for a night. The reaction mixture was distributed into the ethyl acetate and water layers. The organic layer was washed with water, dried and concentrated, and the residue was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 7mg of the subject compound.

25 ¹H-NMR (400MHz, CDCl₃) ; δ (ppm) 7.22(dd, 1H), 7.33-7.35(m, 3H), 7.46-7.60(m, 8H), 7.75(dt, 1H), 8.26(d, 1H), 8.34(d, 1H), 8.60(ddd, 1H).

Example 162.

30 5-(5-Acetoxy-pyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

(162a) 3-(2-Cyanophenyl)-1-phenyl-5-(tri-n-butyl stannyl)-1,2-dihydropyridin-2-one

- 35 [0290] 5.50g of 5-bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one, 45.5g of bis(tributyl tin) and 907mg of tetrakis(triphenylphosphine) palladium were added to 60ml of xylene, and the mixture was stirred at 120°C in a nitrogen atmosphere for 40 minutes. The reaction mixture was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 3.42g of the subject compound.

¹H-NMR (400MHz, CDCl₃) ; δ (ppm) 0.90(t, 9H), 1.07-1.11(m, 6H), 1.30-1.39(m, 6H), 1.52-1.60(m, 6H), 7.29(d, 1H), 7.39-7.47(m,5H), 7.49-7.52(m, 2H), 7.60(d, 1H), 7.71-7.75(m, 2H). (162b) 5-(5-acetoxy-pyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

- 40 [0291] 3.42g of 3-(2-cyanophenyl)-1-phenyl-5-(tri-n-butyl stannyl)-1,2-dihydropyridin-2-one, 1.57g of 5-acetoxy-2-chloropyridine and 352mg of tetrakis(triphenylphosphine) palladium were added to 40ml of xylene, and the mixture was stirred at 120°C in a nitrogen atmosphere for 8.5 hours. The reaction mixture was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 953mg of the subject compound.

45 ¹H-NMR (400MHz, CDCl₃) ; δ (ppm) 2.36(s,3H), 7.44-7.56(m,6H), 7.62-7.68(m,3H), 7.77-7.80(m,2H), 8.27(d,1H), 8.28(d,1H), 8.40(dd,1H).

Example 163.

50 3-(2-Cyanophenyl)-5-(5-hydroxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- [0292] 953mg of 5-(5-acetoxy-pyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one and 192mg of potassium carbonate were added to 50ml of methanol, and the mixture was stirred at room temperature for 30 minutes. The mixture was further incorporated with 50ml of methanol, and stirred at 40°C for 15 minutes. The reaction mixture was diluted with ethyl acetate, and filtered by silica gel. The filtrate was concentrated under a vacuum and washed with a ether/methanol-based solvent, to obtain 786mg of the subject compound.

¹H-NMR (400MHz, DMSO-d₆) ; δ (ppm) 7.19(dd, 1H), 7.49-7.52(m, 1H), 7.55-7.61(m, 5H), 7.71(dd, 1H), 7.78(dt, 1H), 7.82(d, 1H), 7.93(dd, 1H), 8.14(d, 1H), 8.34(d, 1H), 8.37(d, 1H).

Example 164.

3-(2-Cyanophenyl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

[0293] 63mg of 2-tributyl tin pyrimidine, prepared in accordance with Tetrahedron 50(1), 275, (1994), 50mg of 5-bromo-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one and 5mg tetrakis(triphenylphosphine) palladium were added to 2ml of xylene, and the mixture was stirred at 120°C in a nitrogen atmosphere for a night. The reaction mixture was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 10mg of the subject compound. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.15(t, 1H), 7.44-7.54(m, 6H), 7.64(dt, 1H), 7.72-7.78(m, 2H), 8.70(s, 1H), 8.71(s, 1H), 8.72(d, 1H), 8.76(d, 1H).

Example 165.

3-(2-Hydroxypyridin-6-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0294] 20mg of 3-(2-methoxypyridin-6-yl)-1-phenyl-5-(pyridin-2-yl)-1,2-dihydropyridin-2-one is added to 3ml of 5N hydrochloric acid. The mixture was heated under reflux for 3 hours, to which 0.5ml of concentrated hydrochloric acid was added, and further stirred for 1 hour. The reaction mixture was concentrated under a vacuum and washed with ether, to quantitatively obtain the subject compound. ¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.44(d, 1H), 7.08(brs, 1H), 7.47(dd, 1H), 7.52-7.62(m, 6H), 8.02-8.06(m, 1H), 8.18(d, 1H), 8.62(d, 1H), 8.68(dd, 1H), 8.82(dd, 1H).

Example 166.

1-(2-Aminobenzothiazol-6-yl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0295] 150mg of 1-(3-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 63mg of ammonium thiocyanate were added to 2ml of acetic acid. The mixture was stirred at room temperature for 1 hour, to which 0.022ml of bromine was added, and further stirred for 1 hour. The reaction mixture was distributed into the ethyl acetate and water layers, and neutralized with 20% aqueous solution of potassium carbonate. The organic layer was washed with water, dried and concentrated, and the residue was refined by silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 58mg of the subject compound. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 5.37(brs, 1H), 6.76(d, 1H), 7.20-7.24(m, 1H), 7.41-7.80(m, 8H), 8.28-9.40(m, 2H), 8.59-8.61(m, 1H).

Example 167.

1,3-Diphenyl-4-methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0296] The subject compound was obtained, at a yield of 27%, in accordance with the method for Referential Examples 4, 5 and 6 and Example 32 from 2,5-dibromo-4-methylpyridine. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.10(s, 3H), 7.27(ddd, 1H), 7.30-7.51(m, 12H), 7.76(ddd, 1H), 8.66-8.70(m, 1H).

Example 168.

1-Phenyl-3-[(N'-phenylurelylenyl)]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0297] 50mg of 3-amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 25mg of phenyl isocyanate were dissolved in 1ml of tetrahydrofuran, and the solution was stirred at room temperature for 2 hours and at 60°C for 2 hours. The reaction solution was left to cool to room temperature, to which diethyl ether was added. The resultant crystal was separated by filtration, to obtain 30mg of the subject compound. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.03-7.14(m, 3H), 7.17-7.33(m, 4H), 7.38-7.44(m, 2H), 7.45-7.50(m, 2H), 7.59(br s, 1H), 7.68-7.76(m, 2H), 8.02(d, 1H), 8.54-8.57(m, 1H), 8.58(br s, 1H), 9.00(d, 1H).

Example 169.

3-Benzoylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0298] 30mg of 3-amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 1ml of methylenechloride and 1ml of pyridine, to which 19mg of benzoyl chloride was added with cooling with ice, and the mixture was stirred at room temperature for a night. The reaction mixture was concentrated, diluted with ethyl acetate, and washed with a saturated aqueous solution of sodium bicarbonate. The organic layer was dried by magnesium sulfate, and refined by NH silica gel chromatography (ethyl acetate) . The solvent was concentrated, and the resultant crude crystal was
10 washed with ethyl acetate/hexane, to obtain 35mg of the subject compound.
1H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.23(ddd, 1H), 7.47-7.60(m, 8H), 7.70-7.80(m, 2H), 7.95-8.00(m,2H), 8.12(d,1H), 8.57-8.61(m,1H), 9.28(d,1H), 9.35(br s,1H).

Example 170.

3-Benzylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

15 [0299] 40mg of 3-amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 10mg of sodium hydride were added to 1ml of toluene, to which 30mg of benzyl chloride was added dropwise at 70°C. The mixture was stirred for 30 minutes, and heated for 1 hour under reflux. The reaction mixture was left to cool to room temperature, diluted with ethyl acetate, and washed with a water and a saturated saline water. The organic layer was dried by magnesium sulfate, and refined by NH silica gel chromatography (ethyl acetate/hexane-based solvent), to obtain 13mg of the subject compound.
20 1H-NMR (400MHz, CDCl₃) ; δ(ppm) 4.48(d, 2H) , 5.60(br t, 1H) , 6.86(d, 1H) , 7.15(ddd, 1H) , 7.26-7.32(m, 1H) , 7.34-7.40(m, 2H) , 7.40-7.56(m, 9H), 7.66(ddd, 1H), 8.55-8.58(m, 1H).

Example 171.

3-(2-Cyanophenyl)-1-cyclopentyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

30 [0300] 2.00g of 3-bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one as the stock material was N-alkylated by the normal method with 5.94g of bromocyclopentane and 5.50g of potassium carbonate, to obtain 506mg of 3-bromo-1-cyclopentyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one, 150mg of which was treated in accordance with the method for Example 32, to obtain 120mg of the subject compound.
1H-NMR (400MHz,CDCl₃) ; δ(ppm) 1.73-2.02(m,6H), 2.23-2.35(m,2H), 5.37(quintet, 1H), 7.20(ddd, 1H), 7.45(ddd, 1H),
35 7.57(d, 1H), 7.64(ddd, 1H), 7.70-7.79(m, 3H), 8.11(d, 1H), 8.36(d, 1H), 8.59-8.63(m, 1H).

Example 172.

1-{3-[1-(Benzyloxycarbonyl)piperidin-4-yl-oxy]phenyl}-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

40 [0301] 0.99g of 3-bromo-1-(3-hydroxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one was obtained in accordance with the method for Example 18 from 1.02g of 3-bromo-1-(3-methoxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one, synthesized in accordance with the method for Referential Example 6. It was dissolved 30ml of tetrahydrofuran and 10ml of N,N-dimethylformamide, to which 1.52g of triphenyl phosphine and 1.36g of N-benzyloxycarbonyl-4-piperidinol
45 were added, and further 2.52g of a 40% toluene solution of diethylazodicarboxylate was added dropwise with cooling with ice, and the mixture was stirred at room temperature for a night. The reaction solution was concentrated under a vacuum and refined by silica gel chromatography (ethyl acetate/hexane-based solvent) to obtain 0.98g of 1-{3-[N-(benzyloxycarbonyl)piperidin-4-yl-oxy]phenyl}-3-bromo-5-(2-pyridyl)-1,2-dihydropyridin-2-one, from which 0.85g of the subject compound was obtained in accordance with the method for Example 32.
50 1H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.73-1.87(m,2H), 1.88-2.02(m,2H), 3.43-3.52(m,2H), 3.70-3.80(m,2H), 4.50-4.58(m,1H), 5.14(s,2H), 6.98-7.02(m, 1H), 7.06-7.11(m, 2H), 7.22(dd, 1H), 7.30-7.38(m,5H), 7.40-7.49(m,2H), 7.60(ddd,1H), 7.64(ddd,1H), 7.72-7.80(m, 3H), 8.29(d, 1H), 8.31(d, 1H), 8.58-8.61(m, 1H).

55

Example 173.

3-(2-Cyanophenyl)-5-(2-pyridyl 1-oxide)-1-phenyl-1,2-dihydropyridin-2-one

5 [0302] 1.00g of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 30ml of chloroform, to which 0.99g of 60% m-chloroperbenzoic acid was added, and the mixture was stirred at room temperature for 2 hours. Another 1.00g of 60% m-chloroperbenzoic acid was added to the mixture, and the mixture was stirred for 3 hours. The reaction solution was incorporated with 50ml of an aqueous solution of 1N sodium hydroxide, and extracted with ethyl acetate. The organic layer was washed with saturated saline water, dried by magnesium sulfate anhydride,
10 and the solvent was distilled off under a vacuum. The residue was recrystallized from ethyl acetate/diethyl ether, to obtain 0.46g of the subject compound. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21-7.27(m, 1H), 7.36(dt, 1H), 7.43-7.48(m, 2H), 7.50-7.54(m, 4H), 7.61(dd, 1H), 7.63(dt, 1H), 7.78(dd, 1H), 7.81-7.85(m, 1H), 8.10(d, 1H), 8.21(dd, 1H), 8.83(d, 1H).

15 Example 174.

3-Phenylamino-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

20 [0303] 53mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 23mg of aniline were dissolved in 10ml of toluene, to which 2mg of palladium acetate, 7mg of 1,1'-bis(diphenylphosphino)ferrocene and 23mg of sodium tert-butoxide were added, and the mixture was stirred at 110°C for a night. The reaction solution was cooled to room temperature, filtered by silica gel and washed with ether, and the filtrate was distilled under a vacuum to remove the solvent. The residue was refined by silica gel chromatography (NH silica) (hexane/ethyl acetate-based solvent), to obtain 47mg of the subject compound.
25 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.06(tt, 1H), 7.15-7.19(m, 2H), 7.29-7.31(m, 2H), 7.38(tt, 2H), 7.43-7.56(m, 5H), 7.67(d, 1H), 7.69(td, 1H), 7.75(d, 1H), 8.58(ddd, 1H).
ESI-Mass; 340 [M⁺+H]

Example 175.

30

3-Phenoxy-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0304] 100mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 58mg of phenol were dissolved in 10ml of dimethylformamide, to which 84mg of potassium carbonate and 6mg of copper iodide were added, and the
35 mixture was stirred at 150°C for 5 hours. The reaction solution was cooled to room temperature, to which ammonia water was added, and extracted with ethyl acetate. The organic layer was washed with saturated saline water and dried by magnesium sulfate anhydride, and the solvent was distilled off under a vacuum. The residue was refined by silica gel chromatography (hexane/ethyl acetate-based solvent), to obtain 66mg of the subject compound.
40 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.13-7.19(m, 3H), 7.26-7.27(m, 2H), 7.36-7.54(m, 7H), 7.60-7.61(m, 1H), 7.66-7.71(m, 1H), 8.03-8.04(m, 1H), 8.54-8.57(m, 1H).
ESI-Mass; 341 [M⁺+H]

Example 176.

45

3-(1-Adamantylamino)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0305] 27mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 130mg of 1-adamantylamine were dissolved in 10ml of dimethylformamide. To the mixture was added 20mg of sodium hydride, followed by stirring at 130°C in nitrogen atmosphere. After the reaction solution was cooled to room temperature, a saturated aqueous solution of ammonium chloride and water were added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 3mg of the title compound.
50 ¹H-NMR(400MHz, CDCl₃); δ(ppm) 1.19-2.29(m, 16H), 7.06-7.33(m, 3H), 7.34-7.61(m, 5H), 7.66-7.69(m, 1H), 8.08-8.11(m, 2H).
55 ESI-Mass; 398 [M⁺+H]

Example 177.

3-[4-(2-Cyanophenyl)piperidin-1-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0306] 29mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 200mg of 1-(2-cyanophenyl)piperazine, followed by heating at 130°C for 72 hours. After the reaction solution was cooled to room temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 8mg of the title compound.
- 10 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.20-3.22(m,4H), 3.50-3.56(m,4H), 7.00-7.13(m,3H), 7.32-7.61(m,10H), 7.79-7.84(m,2H).
ESI-Mass; 434 [M⁺+H]

Example 178.

15

3-(1-Adamantyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0307] 40mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of tetrahydrofuran. To the mixture were added 5mg of [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium (II) and 1.2mg of copper (I) iodide. While stirring the mixture at room temperature in nitrogen atmosphere overnight, 0.4ml of 1-adamantyl zinc bromide (0.5M tetrahydrofuran solution) was added dropwise thereinto. After stirring in nitrogen atmosphere overnight, an aqueous ammonia was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 12mg of the title compound.
- 20 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.44-2.19(m,15H), 7.13(ddd,1H), 7.31-7.55(m,6H), 7.66(td,1H), 7.93(d,1H), 8.05(d,1H), 8.55-8.58(m,1H).
ESI-Mass; 383 [M⁺+H]

Example 179.

30

3-(1,1-Dichlorohexyl-1-hydroxymethyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0308] 13mg of 3-methoxycarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of tetrahydrofuran, followed by the dropwise addition of 0.05ml of cyclohexyl magnesiumchloride (2.0M diethyl ether solution) in nitrogen atmosphere, under ice-cooling and stirring. After the mixture was stirred for 3hr while heating to room temperature, a saturated aqueous solution of ammonium chloride was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 8mg of the title compound.
- 35 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 0.89-1.84(m,20H), 2.72-2.90(m,2H), 7.12-7.06(m,1H), 7.25-7.49(m,8H), 7.59-7.68(m,1H), 8.50-8.54(m,1H).
ESI-Mass; 443 [M⁺+H]

Example 180.

45

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(1-benzyl-1,2,3,6-tetrahydropyridin-5-yl)-1,2-dihydropyridin-2-one

- [0309] 718mg of 3-bromo-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 40ml of acetonitrile. 383mg of benzyl bromide was added thereto, followed by stirring at 70°C overnight. Further, 383mg of benzyl bromide was added thereto, followed by stirring at 70°C for 2 nights. After cooling to room temperature, the mixture was evaporated. The residue was dissolved in 30ml of methanol, followed by cooling to 0°C under stirring. 265mg of sodium borohydride was added thereto, followed by stirring overnight under heating from 0°C to room temperature. Water was added thereto, the solvent was evaporated, and then the residue was extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 550mg of 3-bromo-5-(2-pyridyl)-1-(1-benzyl-1,2,3,6-tetrahydropyridin-5-yl)-1,2-dihydropyridin-2-one. 270mg of the product was dissolved in 20ml of dimethylformamide. 179mg of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 313mg of cesium carbonate and 15mg of tetrakis(triphenylphosphine) palladium were added thereto, followed by stirring at 120°C for 1 hour. After cooling to room

temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 174mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.40(m,2H), 2.70(t,2H), 3.43(d,2H), 3.68(s, 2H), 6.05(t, 1H), 7.21(dd, 1H), 7.24(m, 1H), 7.30(t, 2H), 7.36(d, 2H), 7.44(t, 1H), 7.54(d, 1H), 7.63(t, 1H), 7.70-7.77(m, 3H), 8.19(d, 1H), 8.23(d, 1H), 8.60(dd, 1H).

Example 181.

3-(2-Cyanophenyl)-5-phenylaminocarbonyl-1-phenyl-1,2-dihydropyridin-2-one

[0310] 41mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-cyanophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 5ml of dichloromethane. Under ice-cooling, a solution of 25mg of oxalyl chloride in dichloromethane was added dropwise thereto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise into a solution of 13mg of aniline and 0.03ml of triethylamine in dichloromethane under ice-cooling. After heating to room temperature, it was stirred in nitrogen atmosphere for 3 hours. Under ice-cooling, the mixture was poured into a saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 11mg of the title compound as white crystals.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.15(tt, 1H), 7.33-7.39(m, 2H), 7.55-7.42(m,6H), 7.56-7.60(m,2H), 7.65(td,1H), 7.73-7.79(m,2H), 7.85(brs,1H), 8.06(d,1H), 8.25(d,1H).

Example 182.

3-(2-Cyanophenyl)-5-(1-phenylbenzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0311] 24mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-cyanophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 16mg of oxalyl chloride in dichloromethane was added dropwise thereto. A catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise into a solution of 21mg of N-phenyl-1,2-phenylenediamine in dichloromethane, under ice-cooling. The mixture was heated to room temperature, followed by stirring in nitrogen atmosphere overnight. Dichloromethane was evaporated, 10ml of acetic acid was added, and the mixture was stirred at 100°C for 5 hours. After cooling to room temperature, acetic acid was evaporated. Under ice-cooling, the residue was poured into a saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 18mg of the title compound as white crystals. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.19-7.30(m,4H), 7.33-7.37(m,1H), 7.39-7.43(m,4H), 7.44-7.45(m,1H), 7.46-7.47(m,1H), 7.55-7.61(m,3H), 7.61-7.66(m,2H), 7.68(d,1H), 7.71(dd,1H), 7.81-7.84(m,1H), 7.87(d,1H).

ESI-Mass; 465 [M⁺+H]

Example 183.

3-(2-Chlorophenyl)-5-(2-benzothiazolyl)-1-phenyl-1,2-dihydropyridin-2-one

[0312] 19mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-chlorophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one (synthesized from 3-bromo-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one and 2-chlorophenylboronic acid in accordance with the method for Referential Example 3) was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 11mg of oxalyl chloride in dichloromethane was added dropwise thereto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise into a solution of 22mg of 2-aminobenzothiol in dichloromethane under ice-cooling. After heating to room temperature, dichloromethane was evaporated. To the residue was added 1ml of polyphosphoric acid, followed by stirring at 180°C overnight. After cooling to room temperature, the reaction mixture was neutralized with 1N aqueous solution of sodium hydroxide and saturated aqueous solution of sodium hydrogen

carbonate under ice-cooling and extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 4mg of the title compound as white crystals. ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.32-7.35(m,2H), 7.37-7.41(m,1H), 7.46-7.51(m,4H), 7.51-7.55(m,4H), 7.87-7.89(m,1H), 8.00(d,1H), 8.14(d,1H), 8.42(d,1H).

ESI-Mass; 415 [M⁺+H]

Example 184.

3-(2-Chlorophenyl)-5-(2-benzoxazolyl)-1-phenyl-1,2-dihydropyridin-2-one

[0313] 19mg of carboxylate obtained by hydrolyzing the ester group of 3-(2-chlorophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one (synthesized from 3-bromo-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one and 2-chlorophenylboronic acid in accordance with the method of Referential Example 3) was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 11mg of oxalyl chloride in dichloromethane was added dropwise thereinto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The solution was added dropwise into a solution of 19mg of 2-aminophenol in dichloromethane under ice-cooling. After heating to room temperature, dichloromethane was evaporated. To the residue was added 1ml of polyphosphoric acid, followed by stirring at 180°C overnight. After cooling to room temperature, the reaction mixture was neutralized with 1N aqueous solution of sodium hydroxide and saturated aqueous solution of sodium hydrogen carbonate under ice-cooling. The mixture was extracted with ethyl acetate, and the resulting organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 3mg of the title compound as white crystals.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.31-7.38(m,4H), 7.45-7.57(m,8H), 7.69-7.71(m,1H), 8.29(d,1H), 8.49(d,1H)

ESI-Mass; 399 [M⁺+H]

Example 185.

3-(2-Chlorophenyl)-5-phenoxyethyl-1-phenyl-1,2-dihydropyridin-2-one

[0314] 24mg of 3-(2-Chlorophenyl)-5-hydroxymethyl-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of tetrahydrofuran. 9.4mg of phenol, 33mg of triphenylphosphine polymer (3mmol/g resin) and 17mg of 1,1'-azobis(N,N-dimethylformamide) were added thereto, followed by stirring at 60°C overnight. Further, 50mg of triphenylphosphine polymer (3mmol/g resin) and 30mg of 1,1'-azobis(N,N-dimethylformamide) were added, followed by stirring at 60°C overnight. After cooling to room temperature, ethyl acetate was added thereto and the triphenylphosphine polymer was removed by filtration through Celite. The filtrate was washed with water and 1N aqueous solution of sodium hydroxide. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 12mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.87(s, 2H), 6.97(dd, 2H), 7.01(dd,1H), 7.26-7.34(m,4H), 7.40-7.51(m,7H), 7.54-7.56(m, 1H), 7.60(d,1H).

ESI-Mass; 388 [M⁺+H]

Example 186.

3-(2-Cyanophenyl)-5-(1-methyl-1,2,3,6-tetrahydropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0315] 99mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of acetonitrile. 2ml of methyl benzenesulfonate was added thereto, followed by stirring at 100°C for 2 nights. After cooling to room temperature, the solvent was evaporated. The residue was dissolved in 10ml of methanol, followed by cooled to 0°C under stirring. Sodium borohydride was added 5 times at intervals of 5 hours, 1g for each time, followed by further stirring at 0°C overnight. Then the solvent was evaporated and a saturated aqueous solution of ammonium chloride was added to the residue, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 107mg of 3-bromo-5-(1-methyl-1,2,3,6-tetrahydropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one. The product was dissolved in 10ml of dimethylformamide. 81mg of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 142mg of cesium carbonate and 7mg of tetrakis(triphenylphosphine) palladium were added thereto, followed

by stirring at 140°C for 2 hours. After cooling to room temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 41mg of the title compound.

5 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.26(s,3H), 2.30-2.50(m,1H), 2.90-2.98(m,1H), 3.15(dd,1H), 3.31-3.40(m,1H), 3.85(t,1H), 5.72-5.78(m,1H), 5.79-5.85(m,1H), 7.40(d,1H), 7.40-7.57(m,5H), 7.60(td,1H), 7.64-7.70(m,1H), 7.72-7.73(m,1H), 7.74-7.75(m,1H), 7.76(d,1H).

Example 187.

10

3-(2-Pyridylethenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0316] 23mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of acetonitrile. To the mixture were added 0.2mg of palladium acetate, 4.3mg of tri-*o*-tolylphosphine and 0.04ml of triethylamine, followed by stirring at 110°C in nitrogen atmosphere overnight. To the mixture was added 9.2mg of 2-vinylpyridine, followed by stirring at 110°C in nitrogen atmosphere for 5 hours. After cooling to room temperature, the reaction mixture was poured into water, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 2mg of the title compound.

15

20 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.12-7.16(m,1H), 7.18-7.23(m,1H), 7.36(d,1H), 7.44-7.51(m,3H), 7.51-7.55(m,2H), 7.57-7.60(m,1H), 7.64(dt,1H), 7.70-7.79(m,1H), 7.78-7.82(m,1H), 8.03-8.07(m,1H), 8.24(d,1H), 8.28(d,1H), 8.57-8.63(m,2H).

ESI-Mass; 352 [M⁺+H]

25

Example 188.

3-(4-Chlorophenylthio)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0317] 25mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of dimethylformamide. To the mixture were added 3mg of sodium hydroxide and 2mg of copper iodide, followed by stirring at 150°C in nitrogen atmosphere overnight. After cooling to room temperature, the reaction mixture was poured into water. An aqueous ammonia was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 8mg of the title compound.

30

35 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.17(ddd,1H), 7.30(d,1H), 7.39-7.56(m,9H), 7.61(d,1H), 7.67(td,1H), 8.08(d,1H), 8.52-8.54(m,1H).

ESI-Mass; 391 [M⁺+H]

Example 189.

40

3-(2-Chlorophenyl)-5-cyclohexyl-1-phenyl-1,2-dihydropyridin-2-one

[0318] 30mg of 5-bromo-3-(2-chlorophenyl)-1-phenyl-1,2-dihydropyridin-2-one synthesized from 5-bromo-1-phenyl-3-iodo-1,2-dihydropyridin-2-one and 2-chlorophenyl boronic acid in accordance with the method of Referential Example 3 was dissolved in 20ml of tetrahydrofuran, followed by adding 1mg of [1,3-bis(diphenylphosphino)propane] nickel (II) chloride. Under stirring in nitrogen atmosphere, 0.1ml of cyclohexyl magnesium chloride (2.0M ether solution) was added dropwise thereto. After stirring at room temperature in nitrogen atmosphere overnight, the mixture was heated under reflux for 1 hour. After cooling to room temperature, a saturated aqueous solution of ammonium chloride was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (chloroform/methanol system), to give 6mg of the title compound.

45

50

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.15-1.47(m,5H), 1.53-1.93(m,5H), 2.35(m,1H), 6.99-7.34(m,3H), 7.36-7.60(m,8H).

ESI-Mass; 364 [M⁺+H]

55

Example 190.

3-(1H-Benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

5 [0319] 25mg of carboxylate obtained by de-protecting the ester group of 3-methoxycarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one in a convention manner was dissolved in 20ml of dichloromethane. Under ice-cooling, a solution of 16mg of oxalyl chloride in dichloromethane was added dropwise thereto and a catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature in nitrogen atmosphere for 1 hour. The reaction solution was evaporated, and to the residue was added dichloromethane. The solution was added dropwise into a solution of 17mg of o-phenylenediamine in dichloromethane under ice-cooling. After heating to room temperature, the mixture was stirred in nitrogen atmosphere overnight. Dichloromethane was evaporated, followed by adding methanol and heating under reflux for 5 hours. After cooling to room temperature, the reaction mixture was poured into an ice-cooled saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was refined by silica gel chromatography (hexane/ethyl acetate system), to give 1.3mg of the title compound as white crystals. ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.10-7.94(m,13H), 8.57(d,1H), 8.60(m,1H), 9.43(d,1H). ESI-Mass; 365 [M⁺+H]

Example 191.

3-(2-Pyridon-1-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

25 [0320] 40mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 23mg of 2-hydroxypyridine were dissolved in 10ml of dimethylformamide. 34mg of potassium carbonate and 3mg of copper iodide were added thereto, followed by stirring at 140°C overnight. After cooling the reaction mixture to room temperature, an aqueous ammonia was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (NH silica) (chloroform/methanol system), to give 10mg of the title compound. ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 6.24(td,1H), 6.69(dd,1H), 7.22(dd,1H), 7.37-7.42(m,2H), 7.45-7.57(m,6H), 7.73(td,1H), 8.33(d,1H), 8.36(d,1H), 8.58-8.60(m,1H).

Example 192.

3-Cyclohexyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

35 [0321] 34mg of 3-bromo-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of tetrahydrofuran, followed by adding 1mg of [1,3-bis(diphenylphosphino)propane] nickel (II) chloride. Under stirring in nitrogen atmosphere, 0.1ml of cyclohexyl magnesium chloride (2.0M ether solution) was added dropwise thereto. The mixture was stirred at room temperature in nitrogen atmosphere for 1 hour, followed by heating under reflux for 72 hours. After cooling to room temperature, water was added thereto, followed by extracting with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (chloroform/methanol system), to give 5mg of the title compound. ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.22-1.52(m,5H), 1.73-1.80(m,1H), 1.81-1.89(m,2H), 1.97-2.04(m,2H), 2.90-2.99(m,1H), 7.18(ddd,1H), 7.53-7.55(m,6H), 7.71(td,1H), 7.78(dd,1H), 8.04(d,1H), 8.59(ddd,1H).

Example 193.

3-[2-(5-Methyl-1,2,4-oxadiazol-3-yl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

50 [0322] 53mg of 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of ethanol containing 20% of water. 19mg of hydroxylamine hydrochloride and 17mg of sodium acetate were added thereto, followed by heating under reflux for 24 hours. Further, 19mg of hydroxylamine hydrochloride and 17mg of sodium acetate were added thereto, followed by heating under reflux for 36 hours. After cooling to room temperature, the mixture was evaporated, and the resulting crystals were washed with water, dried, and 50mg of amidoxime compound was collected by filtration. 20mg of the product was dissolved in 4ml of toluene. 16mg of acetic anhydride was added thereto, followed by heating under reflux for 96 hours. After cooling to room temperature, the mixture was neutralized with potassium carbonate under ice-cooling. After extracting with ethyl acetate, the extract was successively washed with water and brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was

EP 1 300 396 A1

purified by silica gel chromatography (hexane/ethyl acetate system), to give 4mg of the title compound.

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.56(s, 3H), 7.18(ddd, 1H), 7.38-7.59(m, 8H), 7.72(ddd, 1H), 7.71(ddd, 1H), 8.08(ddd, 1H), 8.11(d, 1H), 8.27(d, 1H), 8.58(ddd, 1H).

ESI-Mass; 410 [M⁺+H]

- 5 [0323] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 1.

Example 194.

10 3-(2-Cyanophenyl)-5-(1-methylpyrazol-4-yl)-1-phenyl-1,2 dihydropyridin-2-one

[0324] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.01(s, 3H), 7.46-7.56(m, 8H), 7.62-7.68(m, 3H), 7.78-7.81(m, 2H).

Example 195.

15

3-(2-Cyanophenyl)-5-(6-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0325] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.56(s, 3H), 7.07(d, 1H), 7.40-7.66(m, 9H), 7.76-7.80(m, 2H), 8.28(d, 1H), 8.30(d, 1H).

20

Example 196.

3-(2-Cyanophenyl)-5-(5-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 25 [0326] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.36(s, 3H), 7.42-7.56(m, 8H), 7.63(dt, 1H), 7.76-7.80(m, 2H), 8.26(d, 1H), 8.28(d, 1H), 8.41-8.42(m, 1H).

Example 197.

30 3-(2-Cyanophenyl)-5-(4-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0327] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.36(s, 1H) , 7.43-7.57(m, 8H), 7.63(dt, 1H), 7.77-7.80(m, 2H), 8.27(d, 1H), 8.28(d, 1H), 8.41-8.42(m, 1H).

- 35 Example 198.

3-(2-Cyanophenyl)-5-(3-hydroxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 40 [0328] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.20(dd, 1H), 7.31(dd, 1H), 7.51-7.60(m, 6H), 7.68(dd, 1H), 7.75(dt, 1H), 7.83(dd, 1H), 8.11(dd, 1H), 8.51(d, 1H), 8.55(d, 1H).

Example 199.

3-(2-Cyanophenyl)-1-phenyl-5-(2-pyrazyl)-1,2-dihydropyridin-2-one

45

[0329] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.57(m, 6H), 7.66(dt, 1H), 7.75-7.81(m, 2H), 8.33(d, 1H), 8.35(d, 1H), 8.50(d, 1H), 8.55(dd, 1H), 8.93(d, 1H).

Example 200.

50

3-(2-Cyanophenyl)-5-(2-methoxypyridin-5-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0330] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.69(s,3H), 6.67(d,1H), 7.18(d,1H), 7.44-7.66(m,8H), 7.78-7.81(m,2H), 8.27(d,1H), 8.34(d,1H).

55

EP 1 300 396 A1

Example 201.

3-(2-Cyanophenyl)-1-phenyl-5-(2-thiazoyl)-1,2-dihydropyridin-2-one

5 [0331] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.31(d,1H), 7.45-7.56(m,6H), 7.65(dt,1H), 7.72(dd,1H), 7.77-7.80(m,2H), 8.18(d,1H), 8.25(d,1H).

Example 202.

3-(2-Cyanophenyl)-1-phenyl-5-(4-pyrimidinyl)-1,2-dihydropyridin-2-one

10 [0332] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.59(m,7H), 7.66(dt,1H), 7.76-7.81(m,2H), 8.31(d,1H), 8.56(d,1H), 8.74(d,1H), 9.16(d,1H).

15 Example 203.

3-(2-Cyanophenyl)-1-phenyl-5-(5-pyrimidinyl)-1,2-dihydropyridin-2-one

20 [0333] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.47-7.58(m,6H), 7.66(dt,1H), 7.75(d,1H), 7.78-7.81(m,2H), 7.92(d,1H), 8.92(s,2H), 9.22(s,1H).

Example 204.

3-(2-Cyanophenyl)-1-phenyl-5-(3-pyridazyl)-1,2-dihydropyridin-2-one

25 [0334] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.56(m,7H), 7.66(dt,1H), 7.77-7.83(m,3H), 8.32(d,1H), 8.54(d,1H), 9.15(dd,1H).

Example 205.

3-(2-Cyanophenyl)-1-phenyl-5-(4-pyridazyl)-1,2-dihydropyridin-2-one

30 [0335] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.48-7.61(m, 7H), 7.67(dt, 1H), 7.79-7.83(m, 2H), 7.92(d, 1H), 8.00(d, 1H), 9.23(dd, 1H), 9.40(dd, 1H).

35

Example 206.

3-(2-Cyanophenyl)-5-(2-methoxypyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one

40 [0336] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.96(s, 3H), 6.67(dd, 1H), 7.18(dd, 1H), 7.44-7.66(m, 8H), 7.77-7.81(m, 2H), 8.27(d, 1H), 8.33(d, 1H).

Example 207.

3-(2-Cyanophenyl)-1-phenyl-5-(thiazol-4-yl)-1,2-dihydropyridin-2-one

45 [0337] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.57(m, 6H), 7.66(ddd, 1H), 7.72-7.81(m, 3H), 7.87(d, 1H), 7.97(s, 1H), 8.76(s, 1H).

50 Example 208.

3-(2-Cyanophenyl)-5-(3-oxo-1-cyclohexen-1-yl)-1-phenyl-1,2-dihydropyridin-2-one

55 [0338] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.12-2.19(m,2H), 2.46-2.50(m,2H), 2.65-2.69(m,2H), 6.36(s,1H), 7.45-7.57(m,6H), 7.62-7.70(m,2H), 7.76-7.79(m,2H), 7.88(d,1H).

EP 1 300 396 A1

Example 209.

3-(2-Cyanophenyl)-5-(5,6-dihydro-1,4-dioxin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

5 [0339] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 4.12-4.14(m,2H), 4.21-4.23(m,2H), 7.42-7.78(m,12H).

Example 210.

3-(2-Cyanophenyl)-5-(1-naphthyl)-1-(3-dyridyl)-1,2-dihydropyridin-2-one

10

[0340] ¹H-NMR(400MHz, CDCl₃) ; δ(ppm) 7.41-7.67(m,9H), 7.55-7.83(m,2H), 7.88-7.94(m,2H), 8.02(ddd,1H), 8.11(d,1H) 8.70(d,1H), 8.83(d,1H).

ESI-Mass; 400 [M⁺+H]

15

Example 211.

3-(2-Cyanophenyl)-5-(2-naphthyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

20

[0341] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.44-7.58(m,4H), 7.61-7.70(m,3H), 7.78-7.82(m,2H), 7.83-7.90(m,2H), 7.92(d,1H), 7.95-7.96(m,1H), 8.00(ddd,1H), 8.12(d,1H), 8.72(dd,1H), 8.83(d,1H).

ESI-Mass; 400 [M⁺+H]

Example 212.

25

3-(2-Cyanophenyl)-5-(8-quinoliny)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0342] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.43-7.50(m,3H), 7.60-7.69(m,2H), 7.77(m,1H), 7.81-7.87(m,2H), 8.03-8.10(m,2H), 8.18(d,1H), 8.23(dd,1H), 8.68-8.72(m,2H), 8.87(d,1H), 8.98(dd,1H).

ESI-Mass; 401 [M⁺+H]

30

Example 213.

3-(2-Cyanophenyl)-5-(3-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

35

[0343] ¹H-NMR (400MHz, DMSO-d₆) ; δ(ppm) 7.45-7.51(m, 1H), 7.59(ddd, 1H), 7.64(dd, 1H), 7.75-7.82(m, 2H), 7.94(d, 1H), 8.10(ddd, 1H), 8.15-8.20(m,1H), 8.28(d,1H), 8.39-8.41(m,1H), 8.53-8.56(m,1H), 8.69(dd, 1H), 8.84(d, 1H), 8.98-8.90(m, 1H).

ESI-Mass; 351 [M⁺+H]

40

Example 214.

5-[(1-Benzenesulfonyl)indol-2-yl]-3-(2-cyanophenyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

45

[0344] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 6.70(d, 1H), 7.23-7.43(m, 4H), 7.45-7.56(m, 5H), 7.65(d, 1H), 7.68(td, 2H), 7.78(td, 2H), 7.83(d,1H), 8.02(ddd,1H), 8.30(dd,1H), 8.72(dd,1H), 8.79(d,1H).

ESI-Mass; 529 [M⁺+H]

[0345] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 2.

50

Example 215.

1-(4-Aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

55

[0346] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 3.86(brs, 1H), 6.76(td, 2H), 7.20(ddd, 1H), 7.28(td, 2H), 7.44(dt, 1H), 7.60(td, 1H), 7.64(dd, 1H), 7.71-7.80(m, 3H), 8.28(d, 1H), 8.29(d, 1H), 8.60(ddd, 1H).

EP 1 300 396 A1

Example 216.

5-(3-Aminopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0347] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.05(br s, 2H), 7.07-7.08(m, 2H), 7.42-7.47(m, 2H), 7.51-7.53(m, 4H), 7.62(ddd, 1H), 7.75-7.78(m, 1H), 7.79-7.82(m, 1H), 7.99(dd, 1H), 8.06(dd, 1H), 8.15(dd, 1H).

Example 217.

5-(5-Aminopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

- 10 [0348] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.77(brs, 2H), 7.04(dd, 1H), 7.39-7.52(m, 7H), 7.60-7.64(m, 1H), 7.76-7.80(m, 2H), 8.08(dd, 1H), 8.13(d, 1H), 8.22(d, 1H).

15 Example 218.

1-(3-Aminophenyl)-3-(2-cyanophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

- 20 [0349] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.85(brs, 2H), 6.76(ddd, 1H), 6.84(t, 1H), 6.86(ddd, 1H), 7.14(t, 1H), 7.27-7.31(m, 1H), 7.45(dt, 1H), 7.63(dt, 1H), 7.71-7.78(m, 2H), 8.69-8.71(m, 3H), 8.75(d, 1H).

Example 219.

3-(2-Aminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 25 [0350] ¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.23-7.37(m, 3H), 7.40-7.47(m, 1H), 7.47-7.56(m, 2H), 7.56-7.66(m, 5H), 7.88(ddd, 1H), 8.08(d, 1H), 8.46(d, 1H), 8.58(d, 1H), 8.59-8.64(m, 1H).

Example 220.

3-(3-Aminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 30 [0351] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.70(br s, 2H), 6.68-6.72(m, 1H), 7.13-7.26(m, 3H), 7.42-7.56(m, 5H), 7.56-7.60(m, 1H), 7.64-7.76(m, 2H), 8.22(s, 2H), 8.58-8.61(m, 1H).

35

Example 221.

3-(4-Aminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 40 [0352] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.77(br s, 2H), 6.70-6.76(m, 2H), 7.17-7.21(m, 1H), 7.42-7.60(m, 6H), 7.64-7.75(m, 3H), 8.15(s, 2H), 8.58-8.61(m, 1H).

Example 222.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-aminotoluen-4-yl)-1,2-dihydropyridin-2-one

- 45 [0353] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.21(s, 3H), 3.76(s, 2H), 6.78-6.83(m, 2H), 7.17(d, 1H), 7.20(ddd, 1H), 7.44(td, 1H), 7.58(d, 1H), 7.63(td, 1H), 7.73(td, 1H), 7.78(td, 2H), 8.29(s, 2H), 8.59(ddd, 1H).

ESI-Mass; 379 [M⁺+H]

- 50 [0354] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 3.

Example 223.

3-Benzenesulfonylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 55 [0355] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22(ddd, 1H), 7.31-7.33(m, 2H), 7.44-7.60(m, 7H), 7.76(dt, 1H), 7.92-7.95(m, 2H), 7.97(d, 1H), 8.21(d, 1H), 8.56-8.58(m, 1H).

Example 224.

3-(2-Cyanophenyl)-5-benzenesulfonylamino-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0356] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.26-7.27(m,1H), 7.30-7.33(m,2H), 7.41-7.65(m,10H), 7.70-7.73(m,1H), 7.83-7.86(m,2H).

Example 225.

10 3-(2-Cyanophenyl)-5-[(3-methanesulfonylamino)pyridin-2-yl]-1-phenyl-1,2-dihydropyridin-2-one

- [0357] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 3.40(s,3H), 7.43-7.48(m,4H), 7.50-7.54(m,4H), 7.64-7.66(m,2H), 7.74(dd, 1H), 7.95(d,1H), 8.20(d,1H), 8.77(dd,1H).

15 Example 226.

3-[2-(Methylsulfonylamino)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 20 [0358] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.96(s,3H), 7.25(ddd,1H), 7.30-7.35(m, 1H), 7.43-7.63(m,9H), 7.76(ddd, 1H), 8.30(br s, 1H), 8.33(d,1H), 8.39(d,1H), 8.60-8.64(m,1H).

Example 227.

25 3-[4-(Methanesulfonylamino)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- [0359] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 3.01(s, 3H), 6.57(br s, 1H), 7.20-7.28(m,3H), 7.45-7.61(m,6H), 7.77(ddd, 1H), 7.79-7.85(m,2H), 8.22(d,1H), 8.24(d,1H), 8.60-8.64(m,1H).

Example 228.

30

3-[3-(Methanesulfonylamino)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- [0360] ¹H-NMR(400MHz,CDCl₃) ; δ(ppm) 2.92(s,3H), 6.98(br s, 1H), 7.20-7.32(m,2H), 7.36-7.61(m,8H), 7.69-7.78 (m,2H), 8.22(d,1H), 8.26(d,1H), 8.59-8.63(m,1H).

- 35 [0361] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 11.

Example 229.

40 5-[(6-Acetylaminopyridin-2-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0362] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.22(s,3H), 7.33(dd,1H), 7.44-7.80(m,10H), 7.85(d,1H), 8.08-8.12(m, 1H), 8.24(d,1H), 8.28(d, 1H).

45 Example 230.

3-[2-(Acetylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 50 [0363] ¹H-NMR (400MHz, DMSO-d₆) ; δ(ppm) 1.96(s,3H), 7.19-7.26(m,1H), 7.30(ddd,1H), 7.34-7.40(m,1H), 7.40-7.46(m,1H), 7.48-7.56(m,1H), 7.56-7.64(m,4H), 7.72(d,1H), 7.83(ddd,1H), 8.01(d,1H), 8.32(d,1H), 8.50(d,1H), 8.57-8.61(m,1H), 9.16(br s,1H).

Example 231.

55 3-[2-(Diacetylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- [0364] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.28(s, 6H), 7.18(ddd, 1H), 7.23-7.27(m, 1H), 7.42-7.60(m, 9H), 7.71 (ddd, 1H), 7.95(d, 1H), 8.35(d, 1H), 8.54-8.58(m, 1H).

EP 1 300 396 A1

Example 232.

3-[3-(Acetylamino)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0365] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.11(s,3H), 7.19-7.23(m,1H), 7.34-7.40(m,1H), 7.42-7.56(m,6H), 7.60(d, 1H), 7.64-7.77(m,3H), 7.83-7.87(m,1H), 8.24(d,1H), 8.26(d,1H), 8.58-8.62(m,1H).

Example 233.

3-[4-(Acetylamino)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0366] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.15(s, 3H), 7.21(ddd, 1H), 7.34(br s, 1H), 7.44-7.57(m, 8H), 7.59(ddd, 1H), 7.74(ddd, 1H), 7.80(d, 1H), 8.21(s, 2H), 8.59-8.62(m, 1H).

15 [0367] The following compound was synthesized by the method similar to, or in accordance with, the method for Example 12.

Example 234.

3-(4-Dimethylaminophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

20 [0368] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.00(s, 6H), 6.75-6.80(m, 2H), 7.19(ddd,1H), 7.41-7.54(m,5H), 7.57-7.60 (m,1H), 7.73(ddd,1H), 7.76-7.81(m, 2H), 8.14-8.17(m, 2H), 8.58-8.61(m, 1H).

[0369] The following compound was synthesized by the method similar to, or in accordance with, the method for Example 15.

25

Example 235.

5-[(6-Aminocarbonyl)pyridin-2-yl]-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

30 [0370] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.60(m, 6H), 7.64(dt, 1H), 7.74(dd,1H), 7.80-7.83(m,1H), 7.91-7.95 (m,2H), 8.14-8.17(m,2H), 8.52(d,1H).

[0371] The following compounds were synthesized by the methods similar to, or in accordance with, the method of Example 16, Route 1.

35 Example 236.

3-(2-Cyanophenyl)-5-(2-cyanopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one

40 [0372] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.57(m, 6H), 7.60(dd, 1H), 7.66(dt, 1H), 7.79-7.83(m, 3H), 7.89(dd, 1H), 8.29(d, 1H), 8.41(d, 1H).

Example 237.

3-(3-Hydroxyphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

45

[0373] ¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.74-6.78(m,1H), 7.15-7.26(m,3H), 7.27-7.32(m, 1H), 7.47-7.61(m, 5H), 7.83(ddd, 1H), 8.02(d, 1H), 8.41(s, 2H), 8.57-8.62(m, 1H), 9.43(br s, 1H).

Example 238.

50

3-(4-Hydroxyphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0374] ¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.79-6.84(m, 2H), 7.28(ddd, 1H), 7.47-7.59(m, 5H), 7.61-7.66(m, 2H), 7.82(ddd, 1H), 8.00(d, 1H), 8.33(d, 1H), 8.35(d, 1H), 8.57-8.61(m, 1H), 9.57(br s, 1H).

55 [0375] The following compounds were synthesized by the same methods as in Example 19.

EP 1 300 396 A1

Example 239.

3-(2-Cyanophenyl)-1-[3-(dimethylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0376] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.34(s, 6H), 2.74(t, 2H), 4.10(t, 2H), 7.01-7.05(m, 1H), 7.07-7.11(m, 2H), 7.21(ddd, 1H), 7.42(dd, 1H), 7.45(ddd, 1H), 7.59-7.66(m, 2H), 7.72-7.81(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

Example 240.

3-(2-Cyanophenyl)-1-[3-(piperidinoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

10 [0377] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.39-1.48(m,2H), 1.56-1.64(m,4H), 2.46-2.56(m,4H), 2.78(t,2H), 4.14(t, 2H), 6.99-7.03(m,1H), 7.06-7.11(m, 2H), 7.21(ddd, 1H), 7.41(dd, 1H), 7.45(ddd, 1H) , 7.59-7.66(m, 2H), 7.72-7.81(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

15

Example 241.

3-(2-Cyanophenyl)-1-[3-(pyrrolidinoethoxy)phenyl]-5-(2 pyridyl)-1,2-dihydropyridin-2-one

20 [0378] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.76-1.86(m,4H), 2.57-2.70(m,4H), 2.92(t,2H), 4.16(t,2H), 7.03(ddd,1H), 7.06-7.11(m,2H), 7.21(ddd,1H), 7.41(dd,1H), 7.45(ddd,1H), 7.59-7.66(m,2H), 7.72-7.81(m,3H), 8.30(s,2H), 8.58-8.61(m,1H).

Example 242.

25

3-(2-Cyanophenyl)-1-[3-(diisopropylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

30 [0379] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.03(d,12H), 2.83(t,2H), 3.04(heptet,2H), 3.92(t,2H), 6.97-7.01(m,1H), 7.04(dd,1H), 7.07(ddd,1H), 7.21(ddd,1H), 7.41(dd,1H), 7.45(ddd,1H), 7.59-7.66(m,2H), 7.72-7.82(m,3H), 8.29-8.32(m,2H), 8.58-8.61(m,1H).

Example 243.

3-(2-Cyanophenyl)-1-[3-(dimethylaminopropoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

35

[0380] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.96(tt,2H), 2.24(s,6H), 2.44(t,2H), 4.05(t,2H), 7.00(ddd,1H), 7.05-7.09(m,2H), 7.21(ddd,1H), 7.41(dd,1H), 7.45(ddd,1H), 7.59-7.66(m,2H), 7.72-7.81(m,3H), 8.30(s,2H), 8.58-8.61(m,1H).

Example 244.

40

3-(2-Cyanophenyl)-1-[3-(piperidinopropoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

45 [0381] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.37-1.50(m,2H), 1.53-1.64(m,4H), 1.97(tt,2H), 2.30-2.45(m,4H), 2.47(t, 2H), 4.04(t,2H), 6.97-7.02(m,1H), 7.04-7.09(m,2H), 7.21(ddd,1H), 7.41(dd,1H), 7.45(ddd,1H), 7.59-7.66(m,2H), 7.70-7.82(m,3H), 8.31(s,2H), 8.58-8.62(m,1H).

Example 245.

3-(2-Cyanophenyl)-1-[3-(morpholinoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

50

[0382] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.48-2.65(m,4H), 2.81(t,2H), 3.68-3.80(m,4H), 4.15(t,2H), 6.99-7.04(m, 1H), 7.06-7.13(m,2H), 7.22(ddd,1H), 7.42(dd,1H), 7.46(ddd,1H), 7.61(dd,1H), 7.64(ddd,1H), 7.74(ddd,1H), 7.78(dd, 2H), 8.28-8.33(m,2H), 8.58-8.62(m,1H).

55

EP 1 300 396 A1

Example 246.

3-(2-Cyanophenyl)-1-[3-(diethylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0383] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.07(t,6H) 2.64(q,4H), 2.89(t,2H), 4.08(t,2H), 7.01(ddd,1H), 7.05-7.10(m, 2H), 7.21(ddd,1H), 7.41(dd,1H) 7.45(ddd,1H), 7.59-7.66(m,2H), 7.72-7.81(m,3H), 8.31(s,2H), 8.58-8.61(m,1H).

Example 247.

3-[3-(Dimethylaminoethoxy)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

10 [0384] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.34(s,6H), 2.74(t,2H), 4.13(t,2H), 6.92-6.98(m,1H), 7.19-7.24(m,1H), 7.33(dd,1H), 7.37-7.42(m,1H), 7.44-7.56(m,6H), 7.57-7.62(m,1H), 7.75(ddd,1H), 8.25(s,2H), 8.59-8.63(m,1H).

15 Example 248.

3-[4-(Dimethylaminoethoxy)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

20 [0385] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.35(s,6H), 2.76(t,2H), 4.12(t,2H), 6.95-7.00(m,2H), 7.20(ddd,1H), 7.43-7.54(m,5H), 7.59(ddd,1H), 7.73(ddd,1H), 7.76-7.81(m,2H), 8.17-8.20(m,2H), 8.59-8.62(m,1H).

Example 249.

3-(2-Cyanophenyl)-1-[3-(4-piperidinobutyl-1-oxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

25 [0386] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.38-1.46(m,2H), 1.54-1.61(m,4H), 1.62-1.71(m,2H), 1.75-1.83(m,2H), 2.30-2.43(m,6H), 4.01(t,2H), 6.97-7.01(m,1H), 7.03-7.08(m,2H), 7.21(ddd,1H), 7.40(dd,1H) 7.45(ddd,1H), 7.59-7.66 (m,2H), 7.72-7.82(m,3H), 8.30(s,2H), 8.58-8.61(m,1H).

30 [0387] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 29.

Example 250.

3-(2-Cyanophenyl)-1-[3-(pyrrolidinomethyl)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

35 [0388] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.74-1.84(m,4H), 2.48-2.58(m,4H), 3.69(s,2H), 7.14-7.25(m,2H), 7.38-7.51(m,4H), 7.61(d,1H), 7.63(ddd,1H), 7.72-7.82(m,3H), 8.30(d,1H), 8.32(d,1H), 8.58-8.62(m,1H).

Example 251.

1-[3-[(4-Acetyl)piperazino)methyl]phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

40 [0389] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.07(s,3H), 2.45(dd,4H), 3.45(dd,2H), 3.58(s,2H), 3.63(dd,2H), 7.22(ddd, 1H), 7.40-7.54(m,5H), 7.60-7.67(m,2H), 7.73-7.80(m,3H), 8.29(d,1H), 8.33(d,1H), 8.58-8.62(m,1H).

45 [0390] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 32.

Example 252.

3-(2-Cyanophenyl)-1-(4-nitrophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

50 [0391] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.30(m,1H), 7.47-7.52(m,1H), 7.61-7.82(m,7H), 8.31(dd,1H), 8.42 (d,1H), 8.60-8.63(m,1H).

55

EP 1 300 396 A1

Example 253.

1-Phenyl-3-(2-pyrazyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0392] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21-7.25(m,1H), 7.49-7.59(m,5H), 7.72-7.79(m,2H), 8.46(d,1H), 8.54(d,1H), 8.61(ddd,1H), 8.65(dd,1H), 9.14(d,1H), 9.87(d,1H).

Example 254.

1-Phenyl-3-(2-pyrimidinyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

10 [0393] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20(ddd,1H), 7.25(t,1H), 7.44-7.54(m,4H), 7.66(d,1H), 7.75(dt,1H), 8.45(d,1H), 8.58-8.60(m,1H), 8.82(d,1H), 8.88(s,1H), 8.89(s,1H).

15 Example 255.

1-Phenyl-5-(2-pyridyl)-3-(2-thiazoyl)-1,2-dihydropyridin-2-one

20 [0394] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.26(m,1H), 7.48-7.57(m,6H), 7.78-7.80(m,1H), 8.00(dd,1H), 8.52(dd,1H), 8.59-8.61(m,1H), 9.29(d,1H).

Example 256.

1-Phenyl-3-(4-pyrimidinyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

25 [0395] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.26(m,1H), 7.48-7.59(m,5H), 7.77-7.82(m,2H), 8.53(d,1H), 8.60-8.62(m,1H), 8.73-8.77(m,2H), 9.27(dd,1H), 9.40(d,1H).

Example 257.

1-Phenyl-3-(5-pyrimidinyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

30 [0396] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.27(m,1H), 7.48-7.61(m,7H), 7.77(dt,1H), 8.28(d,1H), 8.37(d,1H), 8.63(ddd,1H), 9.21(d,1H), 9.22(s,1H).

35

Example 258.

1-Phenyl-3-(3-pyridazyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

40 [0397] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.25(m,1H), 7.48-7.58(m,6H), 8.55(d,1H), 8.60(m,1H), 8.78(dd,1H), 9.14(dd,1H), 9.34(d,1H).

Example 259.

1-Phenyl-3-(4-pyridazyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

45 [0398] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.28(m,1H), 7.47-7.62(m,6H), 7.78(dt,1H), 8.16(dd,1H), 8.33(d,1H), 8.53(d,1H), 8.63-8.65(m,1H), 9.23(dd,1H), 9.62(dd,1H).

50 Example 260.

3-(2-Methoxypyridin-6-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

55 [0399] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.07(s,3H), 6.73(dd,1H), 7.46-7.56(m,5H), 7.62-7.70(m,2H), 7.78(ddd,1H), 8.35(dd,1H), 8.39(d,1H), 8.66(ddd,1H), 9.21(d,1H).

Example 261.

3-(2-Cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

5 [0400] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18(t,1H), 7.46-7.52(m,2H), 7.65(dt,1H), 7.71(dd,1H), 7.74-7.80(m,1H), 7.99(ddd,1H), 8.72-8.75(m,5H), 8.82(dd,1H).

Example 262.

10 3-(2-Fulvoropyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

[0401] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.16(t,1H), 7.24-7.27(m,2H), 7.48-7.57(m,5H), 8.19-8.23(m,2H), 8.69-8.76(m,3H).

15 Example 263.

3-(2-Fulvoropyridin-3-yl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

20 [0402] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.19(t,1H), 7.26-7.30(m,1H), 7.47-7.52(m,1H), 7.94(ddd,1H), 8.17(ddd, 1H), 8.70-8.80(m,7H).

Example 264.

3-(2-Cyanopyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

25 [0403] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.17(t,1H), 7.47-7.56(m,6H), 8.14(dd,1H), 8.70(dd,1H), 8.72(d,1H), 8.80 (d,1H), 8.85 (d, 1H).

Example 265.

30

3-(2-Cyanopyridin-3-yl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

[0404] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20(t, 1H), 7.52(ddd, 1H), 7.58(dd, 1H), 7.97(ddd, 1H), 8.11(dd, 1H), 8.71-8.76(m, 4H), 8.78(d, 1H), 8.81(dd, 1H), 8.66(d, 1H).

35

Example 266.

3-(2-Cyanophenyl)-1-(3-nitrophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one

40 [0405] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20(t, 1H), 7.49(ddd, 1H), 7.65-7.80(m, 5H), 7.98(ddd, 1H), 8.36(ddd, 1H), 8.46(t, 1H), 8.73-8.77(m, 4H).

Example 267.

45 1-Phenyl-5-(2-pyridyl)-3-(thiazol-4-yl)-1,2-dihydropyridin-2-one

[0406] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24-7.28(m,1H), 7.48-7.58(m,5H), 7.64(td,1H), 7.79(dt,1H), 8.23(d,1H), 8.58(d,1H), 8.64-8.66(m,2H), 8.85(d,1H).

50 Example 268.

3-(3-Oxo-1-cyclohexen-1-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

55 [0407] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.09-2.16(m,2H), 2.48-2.51(m,2H), 2.87-2.91(m, 2H), 6.53(t, 1H), 7.22 (ddd, 1H), 7.43-7.57 (m, 6H), 7.75(dt, 1H), 8.17(d, 1H), 8.25(d, 1H), 8.60(ddd, 1H).

EP 1 300 396 A1

Example 269.

3-(5,6-Dihydro-1,4-dioxin-2-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0408] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 4.18-4.20(m,2H), 4.30-4.32(m,2H), 7.19(ddd,1H), 7.41-7.54(m,5H), 7.63(td,1H), 7.73(dt,1H), 8.02(s,1H), 8.28(d,1H), 8.58(ddd,1H).

Example 270.

3-(2-Nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

10 [0409] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.22(ddd,1H), 7.40-7.61(m,8H), 7.68(ddd,1H), 7.74(ddd,1H), 8.06(dd,1H), 8.22-8.25(m,2H), 8.60-8.63(m,1H).

15 Example 271.

3-(4-Biphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

20 [0410] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.20-7.25(m,1H), 7.33-7.40(m,1H), 7.42-7.57(m,6H), 7.60-7.79(m,7H), 7.90-7.95(m,2H), 8.25(d,1H), 8.30(d,1H), 8.60-8.64(m,1H).

Example 272.

3-(2-Acetylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

25 [0411] ¹H-NMR (400MHz,CDCl₃) ; δ(ppm) 2.59(s,3H), 7.16-7.21(m,1H), 7.40-7.60(m,8H), 7.63-7.67(m,1H), 7.68-7.75(m,1H), 8.16(d,1H), 8.22(d,1H), 8.57-8.61(m,1H).

Example 273.

30

3-(3-Nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0412] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.24(ddd, 1H) , 7.46-7.64(m, 7H) , 7.76(ddd, 1H), 8.20-8.26(m, 2H), 8.27(d, 1H), 8.37(d, 1H), 8.61-8.65(m, 1H), 8.69(dd, 1H).

35

Example 274.

1-Phenyl-3-(4-pyridyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

40 [0413] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.24(ddd, 1H) , 7.46-7.62(m, 6H) , 7.73-7.81(m, 3H) , 8.28(d, 1H) , 8.39(d, 1H) , 8.61-8.64(m, 1H) . 8.66(dd, 2H).

Example 275.

3-(4-Nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

45 [0414] ¹H-NMR (400MHz,CDCl₃) ; δ(ppm) 7.22-7.26(m,1H), 7.47-7.58(m,5H), 7.60(ddd,1H), 7.76(ddd,1H), 8.01-8.06(m,2H), 8.26-8.31(m,3H), 8.38(d,1H), 8.61-8.65(m,1H).

50 Example 276.

1-[3-(Benzyloxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

55 [0415] ¹H-NMR (400MHz,CDCl₃) ; δ(ppm) 5.10(s,2H), 7.05-7.14(m,2H), 7.17(dd,1H) 7.21(ddd,1H), 7.30-7.48(m, 7H), 7.60(ddd, 1H), 7.64(ddd,1H), 7.71-7.81(m,3H), 8.29-8.32(m,2H), 8.58-8.61(m,1H).

Example 277.

1-(3-Acetylphenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0416] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.66(s, 3H), 7.24(ddd, 1H), 7.48(ddd, 1H), 7.61-7.69(m, 3H), 7.74-7.81(m, 4H), 8.07(ddd, 1H), 8.11(ddd, 1H), 8.32(d, 1H), 8.34(d, 1H), 8.59-8.62(m, 1H).

Example 278.

10 3-[4-(tert-Butylaminosulfonyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0417] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.26(s, 9H), 4.46(s, 1H), 7.24(ddd, 1H), 7.46-7.58(m, 5H), 7.58-7.61(m, 1H), 7.76(ddd, 1H), 7.90-7.99(m, 4H), 8.26(d, 1H), 8.33(d, 1H), 8.61-8.64(m, 1H).

15 Example 279.

3-(1-Naphthyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

20 [0418] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21(dd, 1H), 7.42-7.50(m, 3H), 7.51-7.61(m, 3H), 7.71(td, 1H), 7.81-7.85(m, 1H), 7.87-7.90(m, 2H), 7.96-7.99(m, 1H), 8.20(d, 1H), 8.37(d, 1H), 8.60(d, 1H), 8.67(d, 1H), 8.84(d, 1H).
ESI-Mass; 376 [M⁺+H]

Example 280.

25 3-(1-Naphthyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0419] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.19(ddd, 1H), 7.38-7.59(m, 9H), 7.71(td, 2H), 7.84-7.89(m, 3H), 8.18(d, 1H), 8.39(d, 1H), 8.59(ddd, 1H).
ESI-Mass; 375 [M⁺+H]

30

Example 281.

3-(8-Quinoliny)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

35 [0420] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18-7.23(m, 1H), 7.38-7.56(m, 3H), 7.84-7.58(m, 3H), 7.86-8.01(m, 3H), 8.19-8.23(m, 1H), 8.30-8.36(m, 2H), 8.56-8.62(m, 1H), 8.66-8.70(m, 1H), 8.91-8.97(m, 1H).
ESI-Mass; 377 [M⁺+H]

Example 282.

40

3-(8-Quinoliny)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0421] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18(dd, 1H), 7.39-7.54(m, 4H), 7.55-7.65(m, 3H), 7.66-7.73(m, 2H), 7.85(dd, 1H), 7.98(dd, 1H), 8.2(dd, 1H), 8.34(d, 1H), 8.36(d, 1H), 8.58(d, 1H), 8.94(dd, 1H). ESI-Mass; 376 [M⁺+H]

45

Example 283.

3-(2-Naphthyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

50 [0422] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.23-7.28(m, 1H), 7.48-7.53(m, 3H), 7.64(dt, 1H), 7.78(td, 1H), 7.85-7.91(m, 4H), 7.97(ddd, 1H), 8.25(d, 1H), 8.35(s, 1H), 8.38(d, 1H), 8.64(ddd, 1H), 8.72(d, 1H), 8.81(d, 1H).
ESI-Mass; 376 [M⁺+H]

Example 284.

55

3-(2-Naphthyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0423] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21(dd, 1H), 7.44-7.50(m, 4H), 7.53-7.56(m, 3H), 7.62(dd, 1H), 7.72-7.77

EP 1 300 396 A1

(m, 1H), 7.83-7.91(m, 2H), 7.92(td, 2H), 8.25(d, 1H), 8.37(d, 1H), 8.39(brs, 1H), 8.61-8.64(m, 1H).

Example 285.

5 3-(2-Pyrrolidinopyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0424] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.00-2.04(m, 4H), 3.50(t, 4H), 7.74-7.78(m, 9H), 8.03(d, 1H), 8.06(d, 1H), 8.21(d, 1H), 8.57-8.60(m, 2H).

ESI-Mass; 396 [M⁺+H]

10

Example 286.

3-(2-Formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

15 [0425] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21-7.29(m, 2H), 7.46-7.57(m, 6H), 7.73(d, 1H), 7.75(td, 1H), 8.22(d, 1H), 8.31(d, 1H), 8.60-8.62(m, 1H), 10.00(s, 1H).

ESI-Mass; 359 [M⁺+H]

Example 287.

20

3-(2-Chloropyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0426] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.24(ddd, 1H), 7.37(d, 1H), 7.44-7.51(m, 3H), 7.53-7.60(m, 2H), 7.64-7.70(m, 1H), 7.76(td, 1H), 8.24(d, 1H), 8.26(t, 1H), 8.31(d, 1H), 8.62(ddd, 1H), 8.75(d, 1H).

25 ESI-Mass; 360 [M⁺+H]

Example 288.

3-(2-Fluoropyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

30

[0427] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.99(dd, 1H), 7.24(dd, 1H), 7.47-7.57(m, 5H), 7.59(dd, 1H), 7.76(tdd, 1H), 8.25(dd, 1H), 8.30(dd, 1H), 8.37(td, 1H), 8.57-8.58(m, 1H), 8.63(dt, 1H).

Example 289.

35

3-(2-Ethylthiopyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0428] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.39(t, 3H), 3.20(q, 2H), 7.20-7.24(m, 2H), 7.44-7.59(m, 6H), 7.75(td, 1H), 8.08(dd, 1H), 8.23(d, 1H), 8.26(d, 1H), 8.61(ddd, 1H), 8.78(d, 1H).

40 ESI-Mass; 386 [M⁺+H]

Example 290.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-naphthyl)-1,2-dihydropyridin-2-one

45

[0429] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22(ddd, 1H), 7.47(td, 1H), 7.53-7.60(m, 2H), 7.62-7.67(m, 3H), 7.76(td, 1H), 7.81(td, 2H), 7.88-7.94(m, 2H), 7.98(d, 1H), 7.99(s, 1H), 8.34(d, 1H), 8.43(d, 1H), 8.60(ddd, 1H).

ESI-Mass; 400 [M⁺+H]

Example 291.

50

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(1-naphthyl)-1,2-dihydropyridin-2-one

[0430] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.21(ddd, 1H), 7.45(td, 1H), 7.54-7.65(m, 6H), 7.65-7.83(m, 4H), 7.93-8.02(m, 2H), 8.30(d, 1H), 8.46(d, 1H), 8.57(ddd, 1H).

55

ESI-Mass; 400 [M⁺+H]

EP 1 300 396 A1

Example 292.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(8-quinoliny)-1,2-dihydropyridin-2-one

5 [0431] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.18(ddd, 1H), 7.43(td, 1H), 7.48(dd, 1H), 7.61(td, 1H), 7.63(d, 1H), 7.69(dd, 1H), 7.72(td, 1H), 7.78(dd, 1H), 7.86(dd, 1H), 7.92(dd, 1H), 7.98(dd, 1H), 8.26(dd, 1H), 8.36(d, 1H), 8.43(d, 1H), 8.55-8.57(m, 1H), 8.95(dd, 1H).

Example 293.

10

3-[(1-Benzenesulfonyl)indol-2-yl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0432] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.95(d, 1H), 7.21(ddd, 1H), 7.22(ddd, 1H), 7.26-7.33(m, 3H), 7.42(dt, 1H), 7.44-7.49(m, 2H), 7.50-7.56(m, 4H), 7.60(dt, 1H), 7.71-7.77(m, 3H), 8.07(dd, 1H), 8.20(d, 1H), 8.34(d, 1H), 8.60(ddd, 1H).

15

Example 294.

3-(2-Cyanopyridin-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

20

[0433] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.20-7.28(m, 1H), 7.51(dd, 1H), 7.58(dd, 1H), 7.64(d, 1H), 7.79(td, 1H), 7.94-7.97(m, 1H), 8.18(dd, 1H), 8.35(d, 1H), 8.44(d, 1H), 8.60-8.63(m, 1H), 8.72(dd, 1H), 8.74(dd, 1H), 8.81(d, 1H). ESI-Mass; 352 [M⁺+H]

25

Example 295.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(pyrrol-3-yl)-1,2-dihydropyridin-2-one

[0434] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.46-6.50(m, 1H), 6.79(dd, 1H), 7.21(dd, 1H), 7.29-7.32(m, 1H), 7.45(t, 1H), 7.60-7.66(m, 2H), 7.72-7.80(m, 3H), 8.23(d, 1H), 8.47(d, 1H), 8.61(d, 1H), 8.72(brs, 1H).

30

[0435] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 162.

Example 296.

35

3-(2-Cyanophenyl)-5-(3-nitropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0436] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.43-7.54(m, 7H), 7.62-7.67(m, 2H), 7.73-7.76(m, 2H), 8.03(d, 1H), 8.24(dd, 1H), 8.82(dd, 1H).

40

Example 297.

3-(2-Cyanophenyl)-5-[2-(2,6-dimethylpyrrol-1-yl)pyridin-6-yl]-1-phenyl-1,2-dihydropyridin-2-one

45 [0437] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.17(s, 6H), 5.91(s, 2H), 7.12(dd, 1H), 7.45-7.56(m, 6H), 7.61(dd, 1H), 7.65(dd, 1H), 7.78-7.80(m, 1H), 7.88(t, 1H), 8.35(d, 1H), 8.40(d, 1H).

Example 298.

50

5-(2-Aminopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0438] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.44(brs, 2H), 6.43(dd, 1H), 6.96(d, 1H), 7.42-7.54(m, 7H), 7.63(dt, 1H), 7.76-7.78(m, 1H), 8.24(d, 1H), 8.26(d, 1H).

55

EP 1 300 396 A1

Example 299.

3-(2-Cyanophenyl)-5-(5-nitropyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0439] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.47-7.59(m, 6H), 7.67(dt, 1H), 7.75-7.82(m, 3H), 8.35(d, 1H), 8.52(dd, 1H), 8.55(d, 1H), 9.39(dd, 1H).

Example 300.

- 10 5-(2-Bromopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

[0440] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.39(dd, 1H), 7.45-7.67(m, 9H), 7.78-7.80(m, 2H), 8.23(d, 1H), 8.34(d, 1H).

- 15 Example 301.

3-(2-Cyanophenyl)-1-phenyl-5-(5-trifluoromethylpyridin-2-yl)-1,2-dihydropyridin-2-one

- 20 [0441] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.46-7.58(m, 6H), 7.63-7.68(m, 1H), 7.72(d, 1H), 7.78-7.81(m, 1H), 7.97(ddd, 1H), 8.33(d, 1H), 8.44(d, 1H), 8.83-8.84(m, 1H).

Example 302.

3-(2-Cyanophenyl)-5-(2-morpholinopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 25 [0442] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.55(t, 2H), 3.83(t, 2H), 6.57(d, 1H), 6.97(d, 1H), 7.43-7.66(m, 8H), 7.77-7.80(m, 2H), 8.18(d, 1H), 8.31(d, 1H).

Example 303.

30

3-(2-Cyanophenyl)-5-(2-methoxycarbonylpyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one

- [0443] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.99(s, 3H), 7.44-7.57(m, 6H), 7.65(dt, 1H), 7.78-7.81(m, 3H), 7.91(t, 1H), 8.04(dd, 1H), 8.30(d, 1H), 8.37(d, 1H).

- 35 [0444] The following compound was synthesized by the method similar to, or in accordance with, the method for Example 164.

Example 304.

- 40 5-[4-(tert-Butylaminosulfonyl)phenyl]-3-(2-cyanophenyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

[0445] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.25(s, 9H), 4.72(br s, 1H), 7.47-7.54(m, 2H), 7.60-7.71(m, 4H), 7.73-7.83(m, 2H), 7.93-8.02(m, 4H), 8.73(dd, 1H), 8.79(d, 1H).

- 45 [0446] The following compound was synthesized by the method similar to, or in accordance with, the method for Example 167.

Example 305.

3-(2-Cyanophenyl)-4-methyl-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

50

[0447] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.12(s, 3H), 7.28(ddd, 1H), 7.38-7.52(m, 8H), 7.59(s, 1H), 7.66(ddd, 1H), 7.75-7.80(m, 2H), 8.66-8.70(m, 1H).

[0448] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 168.

55

EP 1 300 396 A1

Example 306.

1-Phenyl-3-[N-(N'-phenylthioureylenyl)]-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0449] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.19-7.24(m,1H), 7.26-7.36(m,3H), 7.37-7.54(m, 7H), 7.70(d, 1H), 7.78(ddd, 1H), 7.92(br s, 1H), 8.09(d, 1H), 8.55-8.59(m, 1H), 9.33(br s, 1H), 10.03(d, 1H).

Example 307.

3-(2-Cyanophenyl)-1-phenyl-5-[N-(N'-phenylureylenyl)]-1,2-dihydropyridin-2-one

10 [0450] ¹H-NMR (400MHz, DMSO-d₆) ; δ(ppm) 6.95(dd, 1H), 7.25(dd, 1H), 7.41-7.61(m, 8H), 7.65(d, 1H), 7.71(d, 1H), 7.77(dd, 1H), 7.92(d, 1H) , 8.03(d, 1H) , 8.56-8.66(m, 1H) , 9.02-9.10(m, 1H) .

15 Example 308.

3-[4[N-(N'-butylureylenyl)phenyl]]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

20 [0451] ¹H-NMR (400MHz, DMSO-d₆) ; δ(ppm) 0.90(t,3H), 1.32(tt, 2H), 1.42(tt,2H), 3.09(dt,2H), 6.16(br t,1H) 7.29(dd, 1H) 7.44(d,2H), 7.47-7.54(m,1H), 7.54-7.60(m,4H), 7.69(d,2H), 7.82(ddd,1H), 8.02(d,1H), 8.35(d,1H), 8.39(d,1H), 8.53(br s,1H), 8.58-8.61(m,1H).

[0452] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 169.

25 Example 309.

3-(2-Cyanophenyl)-1-phenyl-5-(2-pyridincarbonyl)amino-1,2-dihydropyridin-2-one

30 [0453] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.42-7.54(m,7H), 7.63(ddd,1H), 7.74-7.79(m,3H), 7.92(ddd,1H), 8.20(d, 1H), 8.58(d,1H), 8.59-8.62(m,1H), 9.80(br s,1H).

Example 310.

1-Phenyl-3-[2-(1-pyrrolidino)acetyl]amino-5-(2-pyridyl)-1,2-dihydropyridin-2-one

35 [0454] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.78-1.86(m,4H), 2.66-2.74(m,4H), 3.36(s,2H), 7.20(ddd,1H), 7.44-7.56(m,5H), 7.66(d,1H), 7.75(ddd,1H), 8.07(d,1H), 8.54-8.58(m,1H), 9.12(d,1H), 10.15(br s,1H).

Example 311.

1-Phenyl-3-[3-[1-(4-phenyl)piperadino]]propionylamino-5-(2-pyridyl)-1,2-dihydropyridin-2-one

40 [0455] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.66(t,2H), 2.69-2.76(m,4H), 2.80(t,2H), 3.30-3.36(m,4H), 6.81-6.86(m, 1H), 6.90-6.97(m,2H), 7.18(ddd,1H), 7.22-7.29(m,2H), 7.40-7.53(m,5H), 7.62-7.67(m,1H), 7.73(ddd,1H), 8.03(d,1H), 8.53-8.57(m,1H), 9.11(d,1H), 10.56(br s,1H).

Example 312.

3-(3-pyrrolidinopropionyl)amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

50 [0456] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.80-1.88(m,4H), 2.58-2.67(m,6H), 2.86(t,2H), 7.17(ddd,1H), 7.42-7.54(m,5H), 7.65(d,1H) 7.73(ddd,1H), 8.03(d,1H), 8.53-8.57(m,1H), 9.11(d,1H), 10.91(br s,1H).

[0457] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 170.

55

Example 313.

5-Benzylamino-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0458] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.15(s,2H), 6.70(d,1H), 7.30-7.36(m,1H), 7.36-7.43(m,8H), 7.43-7.49(m,3H), 7.59(ddd,1H), 7.72-7.77(m,2H).

Example 314.

10 3-Dibenzylamino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- [0459] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.52(s,4H), 7.12(ddd,1H), 7.16-7.33(m,10H), 7.37-7.54(m,7H), 7.63(ddd,1H), 7.80(d,1H), 8.50-8.54(m,1H).

15 Example 315.

3-(2-Cyanophenyl)-1-(3-hydroxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 20 [0460] 52mg of 1-[3-(benzyloxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one and 20mg of 5% palladium-carbon were added to 3ml of methanol, followed by stirring at room temperature in hydrogen atmosphere overnight. After the resulting insoluble matters were filtered off, the filtrate was evaporated. The residue was purified by silica gel chromatography (ethyl acetate/hexane system), to give 26mg the title compound.
¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.76(dd,1H), 6.87-6.92(m,1H), 6.93(dd,1H), 7.22-7.30(m,2H), 7.44(ddd,1H), 7.60-7.67(m,2H), 7.73-7.80(m,3H), 8.25(d,1H), 8.32(d,1H), 8.33(br s,1H), 8.59-8.63(m,1H).

- 25 [0461] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 171.

Example 316.

30 1-Benzylloxymethyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- [0462] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.76(s,2H), 5.63(s,2H), 7.22(ddd,1H), 7.26-7.42(m,5H), 7.47(ddd,1H), 7.57(d,1H), 7.64-7.80(m,4H), 8.23(d,1H), 8.34(d,1H) 8.60-8.64(m,1H).

35 Example 317.

3-(2-Cyanophenyl)-1-cyclopentylmethyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 40 [0463] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.32-1.42(m,2H), 1.55-1.64(m,2H), 1.65-1.75(m,2H), 1.76-1.86(m,2H), 2.53(ddd,1H), 4.10(d,2H), 7.21(ddd,1H), 7.45(ddd,1H), 7.58(d,1H), 7.64(ddd,1H), 7.71-7.79(m,3H), 8.16(d,1H), 8.28(d,1H), 8.59-8.63(m,1H).

Example 318.

45 1-[1-(tert-butoxycarbonyl)piperidin-4-yl]methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- [0464] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.22-1.35(m,2H), 1.45(s,9H), 1.68-1.78(m,2H), 2.14-2.27(m,1H), 2.61-2.76(m,2H), 3.90-4.25(m,4H), 7.22(ddd,1H), 7.46(ddd,1H), 7.58(ddd,1H), 7.65(ddd,1H), 7.73(ddd,2H), 7.78(dd,1H), 8.17(d,1H), 8.21(d,1H), 8.59-8.63(m,1H).

50

Example 319.

1-[1-(Benzylloxycarbonyl)piperidin-4-yl]methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 55 [0465] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.25-1.38(m,2H), 1.68-1.81(m,2H), 2.17-2.30(m,1H), 2.70-2.86(m,2H), 3.92-4.08(m,2H), 4.15-4.32(m,2H), 5.12(s,2H), 7.22(ddd,1H), 7.28-7.38(m,5H), 7.46(ddd,1H), 7.57(d,1H), 7.65(ddd,1H), 7.69-7.79(m,3H), 8.17(d,1H) 8.20(d,1H), 8.59-8.62(m,1H).

- [0466] The following compounds were synthesized by the methods similar to, or in accordance with, the method for

EP 1 300 396 A1

Example 174.

Example 320.

5 3-(Pyrrol-1-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0467] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.33(t,2H), 7.22(ddd,1H), 7.36(t,2H), 7.45-7.57(m,6H), 7.74(td,1H), 8.10(d,1H), 8.12(d,1H), 8.61(ddd,1H).

ESI-Mass; 314 [M⁺+H]

10

Example 321.

3-(2-Cyanophenylamino)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

15 [0468] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.06(ddd,1H), 7.21(ddd,1H), 7.41-7.65(m,9H), 7.71(td,1H), 7.76(d,1H), 7.88(d,1H), 8.60(ddd,1H).

ESI-Mass; 365 [M⁺+H]

Example 322.

20

3-(2-Pyridylamino)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0469] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.80-6.86(m, 2H), 7.20(dd, 1H), 7.44-7.58(m, 6H), 7.70(d, 1H), 7.77(td, 1H), 7.87(d, 1H), 7.96(s, 1H), 8.37(d, 1H), 8.59(d, 1H), 9.29(d, 1H).

25 ESI-Mass; 341 [M⁺+H]

Example 323.

3-(1-Isoquinolylamino)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

30

[0470] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.15-7.24(m,3H), 7.46-7.59(m,5H), 7.66(t,1H) , 7.77(d,2H) , 7.80(td,1H), 7.97(d,1H), 8.10(d,1H), 8.25(d,1H), 8.61(d,1H), 9.11(s,1H), 9.60(d,1H). ESI-Mass; 391 [M⁺+H]

Example 324.

35

3-(1-Indazolyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0471] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.52(dt,1H), 7.06(ddd,1H), 7.22(ddd,1H), 7.31(td,1H), 7.36(ddd,1H), 7.43-7.57(m,7H), 7.75(dt,1H), 8.03(s,1H), 8.09(d,1H) 8.50(dd,1H).

40 ESI-Mass; 365 [M⁺+H]

Example 325.

3-(9-Carbazoyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

45

[0472] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.29(m,4H), 7.35-7.63(m,9H), 7.52-7.57(m,1H), 8.12(dd,2H), 8.43(dd,1H), 8.46(dd,1H), 8.61(ddd,1H).

Example 326.

50

3-(Indol-1-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0473] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.68(d, 1H) , 7.17(td, 1H), 7.20-7.26(m, 2H), 7.47-7.55(m, 7H), 7.62(d, 1H), 7.66(d, 1H), 7.74(td, 1H), 8.27(d, 1H), 8.34(d, 1H), 8.61(ddd, 1H).

55 ESI-Mass; 364 [M⁺+H]

Example 327.

3-(2-Methyl-5-phenylpyrrol-1-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

5 [0474] 25mg of 3-amino-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 10ml of toluene. To the mixture were added 20mg of 1-phenyl-1,4-pentandione and 0.2mg of p-toluenesulfonate (hydrate), followed by heating under reflux for 1 hour. After cooling to room temperature, the reaction mixture was poured into a saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The organic layer was washed with
10 brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 12mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.26(s,3H), 6.10(d,1H), 6.34(d,1H), 7.21(tt, 1H), 7.17(ddd, 1H), 7.21-7.27(m, 2H), 7.28-7.32(m, 3H), 7.39-7.54(m, 5H), 7.66(td, 1H), 7.83(d, 1H), 8.31(d, 1H), 8.53 (ddd, 1H).

[0475] The following compounds were synthesized by the method similar to, or in accordance with, the method for Example 327.

Example 328.

3-(2,5-Dimethylpyrrol-1-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

20 [0476] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.16(s, 6H), 5.92(s, 2H), 7.22(ddd, 1H), 7.56-7.43(m, 6H), 7.75(td, 1H), 8.07(d, 1H), 8.37(d, 1H), 8.60(ddd, 1H).

Example 329.

25 3-(2-Cyanophenyl)-1-(piperidin-4-yl)methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0477] The titled compound (382mg) was obtained by catalytically hydrogenating 590mg of 1-[1-(benzyloxycarbonyl)piperidin-4-yl] methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one using in a conventional manner using 10% palladium-carbon.

30 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.22-1.34(m,2H), 1.62-1.77(m,2H), 2.08-2.20(m,1H), 2.55-2.63(m,2H), 3.05-3.13(m,2H), 4.00(d,2H), 7.21(ddd,1H), 7.45(ddd,1H), 7.58(ddd,1H), 7.64(ddd,1H), 7.70-7.79(m,3H), 8.17(d,1H), 8.21(d, 1H), 8.59-8.63(m,1H).

[0478] The following compound was synthesized by the method similar to, or in accordance with, the method for Example 329.

Example 330.

3-(2-Cyanophenyl)-1-[3-(4-piperidylloxy)]phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

40 [0479] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.60-1.73(m,2H), 1.98-2.07(m,2H), 2.69-2.77(m,2H), 3.08-3.17(m,2H), 4.39-4.46(m,1H), 6.98-7.02(m,1H), 7.04-7.09(m,2H), 7.21(ddd,1H), 7.38-7.48(m,2H), 7.58-7.67(m,2H), 7.72-7.81(m, 3H), 8.29-8.32(m,2H), 8.58-8.61(m,1H).

Example 331.

45 1-(1-Benzoylpiperidin-4-yl)methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0480] 30mg of 3-(2-cyanophenyl)-1-(piperidin-4-yl)methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 2ml of chloroform. Under ice-cooling, 0.04ml of triethylamine and 19mg of benzoyl chloride were added thereto, followed
50 by stirring at room temperature for 2 hours. The reaction solution was diluted with chloroform, and washed with a saturated aqueous solution of sodium hydrogen carbonate and brine. The organic layer was dried over magnesium sulfate, and then evaporated and the residue was purified by silica gel chromatography (ethyl acetate/hexane), to give 25mg of the title compound.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.22-1.52(m,2H), 1.65-1.78(m,1H), 1.80-1.98(m,1H), 2.28-2.41(m,1H), 2.70-2.86(m,1H), 2.88-3.06(m,1H), 3.70-3.88(m,1H), 3.90-4.23(m,2H), 4.65-4.87 (m,1H), 7.22(dd,1H), 7.36-7.42(m,5H), 7.46
55 (dd,1H), 7.55-7.60(m,1H), 7.62-7.72(m,2H), 7.72-7.79(m,2H), 8.16(d,1H), 8.22(d,1H), 8.59-8.63(m,1H).

[0481] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 331.

EP 1 300 396 A1

Example 332.

1-(1-Acetylpiperidin-4-yl)methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0482] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.22-1.38(m,2H), 1.75-1.86(m,2H), 2.08(s,3H), 2.20-2.35(m,1H), 2.50-2.60(m,1H), 2.98-3.08(m,1H), 3.79-3.87(m,1H), 3.95(dd,1H), 4.05-4.15(m,1H), 4.61-4.70(m,1H), 7.23(ddd,1H), 7.47(ddd,1H), 7.58(d,1H), 7.63-7.71(m,2H), 7.72-7.80(m,2H), 8.17(d,1H), 8.21(d,1H), 8.59-8.63(m,1H).

Example 333.

10

1-[3-(N-acetylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0483] ¹H-NMR (400MHz,CDCl₃); δ(ppm) 1.77-2.02(m,4H), 2.12(s,3H), 3.37-3.45(m,1H), 3.59-3.72(m,2H), 3.75-3.83(m,1H), 4.57-4.62(m,1H), 7.01(ddd, 1H), 7.07-7.12(m, 2H), 7.22(ddd, 1H), 7.43(dd,1H), 7.46(ddd,1H), 7.61
15 (ddd,1H), 7.64(ddd,1H), 7.72-7.80(m, 3H), 8.29(d, 1H), 8.31(d, 1H), 8.58-8.62(m, 1H).

Example 334.

20

1-[3-(N-benzoylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0484] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.75-2.13(m,4H), 3.30-3.47(m,1H), 3.58-3.72(m,1H), 3.75-3.87(m,1H), 3.88-4.03(m,1H), 4.56-4.68(m,1H), 6.99-7.03(m,1H), 7.07-7.13(m,2H), 7.20-7.25(m,1H), 7.38-7.49(m,7H), 7.59-7.67
(m,2H), 7.72-7.80(m,3H), 8.28(d,1H), 8.31(d,1H), 8.58-8.62(m,1H).

25 Example 335.

1-[1-(Benzenesulfonyl)piperidin-4-yl]methyl-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0485] 30mg of 3-(2-cyanophenyl)-1-(piperidin-4-yl)methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one was dissolved in
30 2ml of chloroform. Under ice-cooling, 0.04ml of triethylamine and 23mg of benzenesulfonyl chloride were added thereto, followed by stirring at room temperature for 2 hours. The reaction solution was diluted with chloroform, and washed with a saturated aqueous solution of sodium hydrogen carbonate and brine. The organic layer was dried over magnesium sulfate, and then evaporated and the residue was purified by silica gel chromatography (ethyl acetate/hexane), to give 30mg of the title compound.

35 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.41-1.60(m,2H), 1.77-1.85(m,2H), 1.95-2.06(m,1H), 2.20-2.31(m,2H), 3.80-3.88(m,2H), 3.98(d,2H), 7.22(dd,1H), 7.45(ddd,1H), 7.48-7.68(m,6H), 7.70-7.79(m,4H), 8.15(d,1H), 8.17(d,1H), 8.59-8.63(m,1H).

[0486] The following compounds were synthesized by the methods similar to, or in accordance with, the method for
Example 335.

40

Example 336.

3-(2-Cyanophenyl)-1-[1-(methanesulfonyl)piperidin-4-yl]methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

45 [0487] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.43-1.56(m,2H), 1.83-1.92(m,2H), 2.17-2.30(m,1H), 2.63-2.72(m,2H), 2.77(s,3H), 3.80-3.88(m,2H), 4.03(d,2H), 7.20-7.26(m,1H), 7.44-7.51(m,1H), 7.55-7.61(m,1H), 7.63-7.72(m,2H), 7.73-7.82(m,2H), 8.17(d,1H), 8.21(d,1H), 8.59-8.64(m,1H).

Example 337.

50

1-[3-[1-(Benzenesulfonyl)piperidin-4-yl-oxy]phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0488] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.90-2.10(m,4H), 3.10-3.23(m,4H), 4.38-4.45(m,1H), 6.87-6.92(m,1H), 6.98(dd,1H), 7.05(ddd,1H), 7.22(ddd,1H), 7.38(dd,1H), 7.46(ddd,1H), 7.52-7.66(m,5H), 7.72-7.80(m,5H), 8.25-8.28
55 (m,2H), 8.57-8.60(m,1H).

Example 338.

3-(2-Cyanophenyl)-1-{3-[1-(methanesulfonyl)piperidin-4-yl-oxy]phenyl}-5-(2-pyridyl)-1,2-dihydropyridin-2-one

5 [0489] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.98-2.10(m, 4H), 2.81(s, 3H), 3.30-3.41(m, 4H), 4.56-4.62(m, 1H), 6.98-7.02(m, 1H), 7.08-7.13(m, 2H), 7.23(ddd, 1H), 7.44(dd, 1H), 7.47(ddd, 1H), 7.61(ddd, 1H), 7.65(ddd, 1H), 7.73-7.80(m, 3H), 8.28(d, 1H), 8.32(d, 1H), 8.59-8.62(m, 1H).

Example 339.

10

3-(2-Cyanophenyl)-1-(1-benzylpiperidin-4-yl)methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0490] 80mg of 3-(2-cyanophenyl)-1-(piperidin-4-yl)methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 2ml of chloroform. To the mixture were added 73mg of benzaldehyde, 97mg of triacetoxy sodium borohydride and 41mg of acetic acid, followed by stirring at room temperature for 4 hours. The reaction solution was diluted with chloroform, and washed with a saturated aqueous solution of sodium hydrogen carbonate and brine. The organic layer was dried over magnesium sulfate. Then the mixture was evaporated, and the residue was purified by NH silica gel chromatography (hexane/ethyl acetate system), to give 80mg of the title compound.

15 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.44(ddd, 2H), 1.68-1.76(m, 2H), 1.92-2.06(m, 3H), 2.37-2.93(m, 2H), 3.48(s, 2H), 4.01(d, 2H), 7.18-7.25(m, 2H), 7.27-7.32(m, 4H), 7.45(ddd, 1H), 7.56(d, 1H), 7.64(ddd, 1H), 7.70-7.78(m, 3H), 8.16(d, 1H), 8.19(d, 1H), 8.58-8.61(m, 1H).

[0491] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 339.

25 Example 340.

3-(2-Cyanophenyl)-1-(1-methylpiperidin-4-yl)methyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

30 [0492] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.38-1.50(m, 2H), 1.65-1.80(m, 2H), 1.88-2.05(m, 3H), 2.25(s, 3H), 2.82-2.92(m, 2H), 4.01(d, 2H), 7.19-7.24(m, 1H), 7.43-7.49(m, 1H), 7.56-7.60(m, 1H), 7.62-7.68(m, 1H), 7.70-7.80(m, 3H), 8.17(d, 1H), 8.20(d, 1H), 8.59-8.63(m, 1H).

Example 341.

35 1-[3-(N-methylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0493] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.80-1.93(m, 2H), 1.97-2.08(m, 2H), 2.23-2.37(m, 5H), 2.60-2.73(m, 2H), 4.33-4.42(m, 1H), 6.97-7.02(m, 1H), 7.04-7.10(m, 2H), 7.19-7.24(m, 1H), 7.38-7.49(m, 2H), 7.58-7.68(m, 2H), 7.72-7.82(m, 3H), 8.28-8.33(m, 2H), 8.58-8.62(m, 1H).

40

Example 342.

1-[3-(N-benzylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one

45 [0494] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.78-1.88(m, 2H), 1.97-2.06(m, 2H), 2.26-2.35(m, 2H), 2.58-2.76(m, 2H), 4.33-4.41(m, 1H), 6.97-7.01(m, 1H), 7.04-7.08(m, 2H), 7.21(ddd, 1H), 7.24-7.28(m, 1H), 7.30-7.34(m, 4H), 7.40(dd, 1H), 7.46(ddd, 1H), 7.60(ddd, 1H), 7.64(ddd, 1H), 7.72-7.80(m, 3H), 8.30(s, 2H), 8.58-8.61(m, 1H).

Example 343.

50

3-(4-Sulfamoylphenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

[0495] 80mg of 3-[4-(tert-butylaminosulfonyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 3ml of trifluoroacetic acid, followed by heating under reflux for 1 hour. It was left to cool to room temperature, and then the reaction mixture was diluted with ethyl acetate/tetrahydrofuran, and washed with a saturated aqueous solution of sodium hydrogen carbonate and brine. The organic layer was dried over magnesium sulfate, and then evaporated. The resulting crude crystals were washed with ethyl acetate, to give 60mg of the title compound.

55 ¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.31(ddd, 1H), 7.49-7.61(m, 5H), 7.82-7.90(m, 3H), 7.97-8.02(m, 2H),

EP 1 300 396 A1

8.03-8.07(m, 1H), 8.48(d, 1H), 8.54(d, 1H), 8.59-8.62(m, 1H).

[0496] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 181.

5 Example 344.

3-Cyclohexylaminocarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

10 [0497] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.12-2.10(m,10H), 3.97-4.04(m,1H), 7.23(ddd,1H), 7.43-7.58(m,1H), 7.49-7.59(m,4H), 7.74-7.77(m,1H), 7.79(td,1H), 8.55-8.56(m,1H), 8.57(d,1H), 9.18(d,1H), 9.64(d,1H).
ESI-Mass; 374 [M⁺+H]

Example 345.

15 3-(2-Cyanophenyl)-5-(1-adamantylaminocarbonyl)-1-phenyl-1,2-dihydropyridin-2-one

[0498] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.77-1.56(m,7H), 1.97-2.15(m,8H), 5.63(s, 1H), 7.42-7.54(m, 6H), 7.63(td, 1H), 7.74-7.78(m, 2H), 7.88(d, 1H), 8.12(d, 1H).

20 Example 346.

3-(1-Adamantylaminocarbonyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

25 [0499] ¹H-NMR(400MHz,CDCl₃);δ(ppm) 1.50-1.72(m,12H), 1.99-2.15(m,3H), 7.21-7.29(m,1H), 7.43-7.49(m,2H), 7.48-7.60(m,4H), 7.75-7.80(m, 1H), 8.47(d, 1H), 8.55(d, 1H), 8.60(ddd, 1H).

Example 347.

30 3-[1-[4-(2-Cyanophenyl)piperadino]carbonyl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0500] ¹H-NMR (400MHz,CDCl₃); δ(ppm) 3.12-3.31(m,4H), 3.59-3.79(m,4H), 6.99-7.06(m,2H), 7.22(dd,1H), 7.27-7.62(m,8H), 7.75(td,1H), 8.29(d,1H), 8.37(d,1H), 8.58(ddd,1H).
ESI-Mass; 462 [M⁺+H]

35 Example 348.

3-[(2-Phenylhydrazino)carbonyl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

40 [0501] ¹H-NMR (400MHz,CDCl₃); δ(ppm) 6.53(d,1H), 6.89(t,1H), 6.94(d,2H), 7.20-7.30(m,3H), 7.62-7.47(m,5H), 7.71-7.77(m,1H), 7.80(dd,1H), 8.56-8.57(m,1H), 8.64(d,1H), 9.16(d,1H), 11.23(d,1H).
ESI-Mass; 383 [M⁺+H]

Example 349.

45 3-Phenylaminocarbonyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0502] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.06-7.17(m, 1H), 7.23-7.28(m,1H), 7.31-7.37(m, 2H), 7.46-7.62(m, 5H), 7.73-7.83(m, 4H), 8.58(ddd,1H), 8.63(d, 1H), 9.29(d, 1H), 11.86(brs, 1H).

50 Example 350.

(350A) 3-(2-Chlorophenyl)-5-(4-chlorobenzenesulfonyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

(350B) 3-(2-Chlorophenyl)-5-(4-chlorobenzenesulfonyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

55

[0503] 38mg of 3-(2-chlorophenyl)-5-(4-chlorophenylthio)-1-(3-pyridyl)-1,2-dihydropyridin-2-one was dissolved in 10ml of dichloromethane. Under ice-cooling, 15.4mg of m-chloroperbenzoic acid was added thereto, followed by stirring at the same temperature for 1 hour. Further, 10mg of m-chloroperbenzoic acid was added thereto, followed by stirring

EP 1 300 396 A1

for 2 hours under ice-cooling. Then, the mixture was diluted with 30ml of ethyl acetate, and washed with an aqueous solution of 1N sodium hydroxide. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 9mg of 3-(2-chlorophenyl)-5-(4-chlorobenzenesulfonyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one and 6mg of 3-(2-chlorophenyl)-5-(4-chlorobenzenesulfonyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one as the title compounds.

(350A)

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.27-7.33(m, 3H), 7.36(d, 1H), 7.40-7.44(m, 1H), 7.48-7.57(m, 3H), 7.63-7.67(m, 2H), 7.87-7.92(m, 1H), 7.97(d, 1H), 8.70-8.76(m, 2H).

ESI-Mass; 441 [M⁺+H]

(350B)

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.30-7.37(m, 2H), 7.44-7.52(m, 3H), 7.56(t, 1H), 7.58(t, 1H), 7.34(d, 1H), 7.84-7.88(m, 1H),

7.89(t, 1H), 7.92(t, 1H), 8.24(d, 1H), 8.71(dd, 1H), 8.75(dd, 1H). ESI-Mass; 457 [M⁺+H]

[0504] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 182.

Example 351.

3-(2-Cyanophenyl)-5-(5-methyl-1H-benzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0505] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.45(s, 3H), 7.05(d, 1H), 7.34-7.43(m, 7H), 7.57(td, 2H), 7.62(ddd, 1H), 7.68(ddd, 1H), 8.18(d, 1H), 8.27(d, 1H).

ESI-Mass; 403 [M⁺+H]

Example 352.

3-(2-Cyanophenyl)-5-(4-methyl-1H-benzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0506] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.50(brs, 1.5H), 2.63 (brs, 1.5H) 7.02(d, 1H), 7.14(t, 1H), 7.30-7.40(m, 7H), 7.52-7.58(m, 2H), 7.65(d, 1H), 8.18-8.23(m, 1H), 8.24(d, 1H).

ESI-Mass; 403 [M⁺+H]

Example 353.

3-(2-Cyanophenyl)-5-(5,6-dichloro-1H-benzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0507] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.39-7.49 (m, 6H), 7.52-7.54 (m, 1H), 7.60-7.66(m, 2H), 7.70-7.72(m, 1H), 7.72-7.74(m, 1H), 8.21(d, 1H), 8.37(d, 1H).

ESI-Mass; 457 [M⁺+H]

Example 354.

3-(5,6-Dichloro-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0508] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.27(ddd, 1H), 7.48-7.63(m, 6H), 7.82(td, 1H), 7.83-7.89(m, 2H), 8.59(d, 1H), 8.60(dt, 1H), 9.38(d, 1H), 12.15(s, 1H).

ESI-Mass; 433 [M⁺+H]

Example 355.

3-(6-Chloro-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0509] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.28(m, 2H), 7.50-7.63(m, 6H), 7.78-7.88(m, 3H), 8.58(dd, 1H), 8.61(ddd, 1H), 9.40(d, 1H).

ESI-Mass; 399 [M⁺+H]

Example 356.

3-[1-(Pyridin-4-yl)benzimidazol-2-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0510] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.10-7.13(m,2H), 7.22-7.28(m,2H) 7.31-7.46(m, 8H), 7.69(dt, 1H), 7.77 (td, 1H), 7.91(dt, 1H), 8.43(d, 1H), 8.59(ddd, 1H), 8.73-8.75(m, 2H).
ESI-Mass; 442 [M⁺+H]

Example 357.

10

3-[1-(1-Benzylpiperidin-4-yl)benzimidazol-2-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 15 [0511] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 2.01-2.20(m,4H), 2.56-2.66(m,2H), 3.02-3.07(m, 2H), 3.58(s, 2H), 4.09-4.18(m, 1H), 7.21(ddd, 1H), 7.24-7.30(m, 3H), 7.31-7.36(m, 2H), 7.45-7.50(m, 4H), 7.52-7.60(m, 3H), 7.64(d, 1H), 7.74(td, 1H), 7.77-7.84(m, 2H), 8.48(d, 1H), 8.49(d, 1H), 8.58(ddd, 1H).
ESI-Mass; 538 [M⁺+H]

Example 358.

20

3-(2-Cyanophenyl)-5-(5,6-dihydro-4H-imidazo[4,5,1-i,j]quinolin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0512] ¹H-NMR(400MHz,CDCl₃);δ(ppm) 2.30(qu,2H), 3.02(t,2H), 4.47(t,2H), 7.04(dd,1H), 7.20(dd,1H), 7.45-7.57 (m,7H), 7.65(td,1H), 7.79(dd,1H), 7.81(dd,1H), 8.10(d,1H), 8.22(d,1H).
ESI-Mass; 429 [M⁺+H]

25

Example 359.

3-(5,6-Dihydro-4H-imidazo[4,5,1-i,j]quinolin-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 30 [0513] ¹H-NMR (400MHz,CDCl₃); δ(ppm) 2.20(qu,2H), 2.98(t,2H), 4.35(t,2H), 7.03(d, 1H), 7.18-7.23(m, 2H), 7.44-7.58(m, 5H), 7.62 (d,1H), 7.70(d,1H), 7.75(dt,1H), 8.52(d,1H), 8.57(ddd,1H), 8.70(d,1H).
ESI-Mass; 405 [M⁺+H]

Example 360.

35

3-(1-Phenylbenzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0514] ¹H-NMR (400MHz,CDCl₃); δ(ppm) 7.05-7.21(m,3H), 7.25-7.45(m,6H), 7.47-7.65(m,7H), 8.10(d,1H), 8.54-8.59(m,1H), 8.85-8.95(m,1H), 9.22(d,1H).
40 ESI-Mass; 441 [M⁺+H]

Example 361.

3-(2-Chlorophenyl)-5-(6-chloro-1H-benzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

45

[0515] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.92(td,1H), 6.97-7.07(m,4H), 7.11-7.14(m,2H), 7.18-7.24(m,3H), 7.25-7.29(m,2H), 7.94(d,1H), 8.24(d,1H).
ESI-Mass; 432 [M⁺+H]

50

Example 362.

3-(2-Cyanophenyl)-5-(1H-imidazo[4,5-c]pyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 55 [0516] ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.04-7.09(m,1H), 7.28-7.31(m,1H), 7.44-7.60(m,5H), 7.66-7.70(m,2H), 7.74-7.78(m,1H), 7.80(d,1H), 7.93-7.96(m,1H), 8.01(d,1H), 8.40(d,1H), 8.51(d,1H).
ESI-Mass; 390 [M⁺+H]

EP 1 300 396 A1

Example 363.

3-(6-Methyl-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

5 [0517] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.50(s, 3H), 7.08-7.15(m, 1H), 7.23-7.26(m, 1H), 7.45-7.69(m, 7H), 7.81 (td, 1H), 7.88(d, 1H), 8.56(d, 1H), 8.59(ddd, 1H), 9.40(d, 1H), 11.95-12.07(m, 1H). ESI-Mass; 379 [M⁺+H]

Example 364.

3-(5-Methyl-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

10 [0518] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.49(s, 3H), 7.12(t, 1H), 7.24-7.27(m, 1H), 7.31-7.72(m, 7H), 7.80(td, 1H), 7.87(d, 1H), 8.56(d, 1H), 8.59(ddd, 1H), 9.40(d, 1H), 11.94-12.07(m, 1H). ESI-Mass; 379 [M⁺+H]

15 Example 365.

3-(2-Cyanophenyl)-5-[1-(1-benzylpiperidin-4-yl)benzimidazol-2-yl]-1-phenyl-1,2-dihydropyridin-2-one

20 [0519] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.92(dd, 2H), 2.36(t, 2H), 2.75(ddd, 2H), 3.05(d, 2H), 3.62(s, 2H), 4.58(tt, 1H), 7.26-7.41(m, 7H), 7.44-7.51(m, 2H), 7.52-7.56(m, 4H), 7.65(td, 1H), 7.70(dd, 1H), 7.72(d, 1H), 7.73-7.81(m, 3H), 8.01(d, 1H).
ESI-Mass; 562 [M⁺+H]

Example 366.

25

3-(2-Cyanophenyl)-5-(5-methoxy-1H-benzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

[0520] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 3.83(s, 3H), 6.85(dd, 1H), 7.24-7.47(m, 8H), 7.50(d, 2H), 7.60(dt, 1H), 8.15(s, 1H), 8.16(s, 1H).
30 ESI-Mass; 419 [M⁺+H]

Example 367.

3-(1H-Imidazo[4,5-c]pyridin-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

35

[0521] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.19-7.28(m, 1H), 7.48-7.63(m, 4H), 7.69-7.90(m, 2H), 8.08(d, 1H), 8.12 (d, 1H), 8.16-8.22(m, 1H), 8.34(d, 1H), 8.59(d, 1H), 8.58-8.62(m, 1H), 9.44(d, 1H), 12.20(brs, 1H).
ESI-Mass; 366 [M⁺+H]

40 Example 368.

3-(2-Cyanophenyl)-5-[1-(pyridin-4-yl)benzimidazol-2-yl]-1-phenyl-1,2-dihydropyridin-2-one

45 [0522] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.29-7.34(m, 4H), 7.35-7.51(m, 8H), 7.59(td, 1H), 7.69(d, 1H), 7.73(dd, 1H), 7.82(d, 1H), 7.84(dt, 1H), 8.91(dd, 2H).
ESI-Mass; 466 [M⁺+H]
[0523] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 183.

50 Example 369.

3-(2-Chlorophenyl)-5-(5-trifluoromethylbenzothiazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

55 [0524] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.32-7.37(m, 2H), 7.47-7.58(m, 7H), 7.61(ddd, 1H), 7.99(d, 1H), 8.14(d, 1H), 8.21-8.23(m, 1H), 8.39(d, 1H).
ESI-Mass; 483 [M⁺+H]

EP 1 300 396 A1

Example 370.

3-(5-Trifluoromethylbenzothiazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

5 [0525] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.26-7.30 (m,1H), 7.51-7.64(m,6H), 7.81-7.87(m, 2H), 8.08(d, 1H), 8.39 (s, 1H), 8.63(d, 1H), 8.64(t,1H), 9.50(d,1H).

ESI-Mass; 450 [M⁺+H]

Example 371.

10

3-(2-Benzothiazolyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0526] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.26-7.30(m, 1H) , 7.41(t, 1H) , 7.50-7.60(m, 6H) , 7.84(t, 1H), 7.88-7.94 (m, 1H) , 7.98(d, 1H) , 8.12(d, 1H), 8.60-8.63(m, 2H), 9.48-9.52(m, 1H).

15 ESI-Mass; 382 [M⁺+H]

Example 372.

5-(2-Benzothiazolyl)-3-[2-(2-benzothiazolyl)phenyl]-1-phenyl-1,2-dihydropyridin-2-one

20

[0527] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.09-7.14(m,2H), 7.25-7.33(m,4H), 7.37(td,1H 7.42(td,1H), 7.46-7.52(m, 4H), 7.80(ddt,2H), 7.90(ddt,2H), 7.95(d,1H), 8.12(d,1H), 8.30(d,1H).

ESI-Mass; 514 [M⁺+H]

25 [0528] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 184.

Example 373.

5-(2-Benzoxazolyl)-3-[2-(2-benzoxazolyl)phenyl]-1-phenyl-1,2-dihydropyridin-2-one

30

[0529] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.22-7.42(m,7H) 7.44-7.73(m,9H), 8.26(d,1H), 8.34(d,1H) 8.48(d,1H).

ESI-Mass; 482 [M⁺+H]

Example 374.

35

3-(2-Benzoxazolyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0530] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.22-7.28(m,1H), 7.29-7.32(m,2H), 7.42-7.46(m,2H), 7.48-7.50(m,3H), 7.54-7.58(m,1H), 7.70-7.80(m,3H), 8.55-8.60(m,2H), 9.03(d,1H).

40 ESI-Mass; 366 [M⁺+H]

Example 375.

3-(2-Chlorophenyl)-5-(5-chlorobenzoxazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

45

[0531] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.27-7.35(m,3H) 7.41-7.51(m,4H), 7.52-7.57(m, 4H), 7.67(d, 1H), 8.25(d, 1H), 8.49(d, 1H).

ESI-Mass; 433 [M⁺+H]

50 Example 376.

3-(5-Chlorobenzoxazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

55 [0532] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.26(ddd, 1H), 7.33(dd, 1H), 7.47-7.58(m, 6H), 7.72(dt, 1H), 7.79(d, 1H), 7.79(td, 1H), 8.55(d, 1H), 8.62(ddd, 1H), 9.12(d, 1H).

ESI-Mass; 340 [M⁺+H]

[0533] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 315.

EP 1 300 396 A1

Example 377.

3-[1-(Piperidin-4-yl)benzimidazol-2-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- 5 [0534] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 2.01-2.15(m,2H), 2.42-2.52(m,2H), 2.66-2.84(m, 2H), 3.20-3.30(m, 2H), 4.21-4.40(m, 1H), 7.19-7.83(m, 12H), 8.49(d, 1H), 8.52(d, 1H), 8.56-8.59(m, 1H).
ESI-Mass; 448 [M⁺+H]

Example 378.

10

(378A) 3-(2-Cyanophenyl)-5-[1-(piperidin-4-yl)benzimidazol-2-yl]-1-phenyl-1,2-dihydropyridin-2-one

(378B) 3-(2-Cyanophenyl)-5-[1-(1-methylpiperidin-4-yl)benzimidazol-2-yl]-1-phenyl-1,2-dihydropyridin-2-one (378A)

- 15 [0535] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.90-2.02(m, 2H) , 2.65(ddd, 2H) , 3.01(t, 2H), 3.28(d, 2H), 4.69(tt, 1H), 7.27-7.29(m, 2H), 7.47-7.55(m, 6H) , 7.67(td, 1H) , 7.71(d, 1H) , 7.67-7.83(m, 4H) , 8.05(d, 1H).
ESI-Mass; 472 [M⁺+H]
(378B)
¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.90-2.00(m,2H), 2.35-2.40(m,2H), 2.41(s, 3H), 2.73-2.87(m, 2H), 3.00-3.10(m, 20 2H), 4.51-4.62(m,1H), 7.26-7.30(m, 2H) , 7.44-7.54(m, 6H) , 7.65(td, 1H) , 7.70-7.83(m, 5H), 8.03(d, 1H) .
ESI-Mass; 486 [M⁺+H]

Example 379.

25

(379A) 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(piperidin-3-yl)-1,2-dihydropyridin-2-one

(379B) 3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(N-benzylpiperidin-3-yl)-1,2-dihydropyridin-2-one

(379A)

30

[0536] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.90-2.05(m,2H) 2.13-2.22(m,1H), 2.35-2.44(m, 1H), 2.70(td, 1H), 3.05-3.12(m, 1H), 3.37(d, 1H), 3.60-3.72(m, 1H), 4.97-5.05(m, 1H), 7.21(ddd, 1H), 7.45(td, 1H), 7.57(d, 1H), 7.64(td, 1H), 7.68-7.78(m, 3H), 8.13(d, 1H), 8.48(d, 1H), 8.62(ddd, 1H).
ESI-Mass; 357 [M⁺+H]

35

(379B)

¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.65-1.75(m,2H), 1.92-2.05(m,2H), 2.45-2.60(m, 2H), 2.70-2.80(m, 1H), 2.97(dd, 1H), 3.55(s, 2H), 5.15-5.20(m, 1H), 7.22(ddd, 1H), 7.27-7.32(m, 1H), 7.40-7.49(m,4H), 7.52-7.5(m, 2H), 7.61-7.77(m, 5H), 8.15(d, 1H), 8.65(ddd, 1H).
ESI-Mass; 447 [M⁺+H]

40

Example 380.

3-(2-Cyanophenyl)-5-(N-methylpiperidin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 45 [0537] ¹H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.24-1.39(m,2H), 1.73-1.85(m,2H), 2.04-2.14(m,3H), 2.16(s,3H), 2.63(dd, 1H), 3.00(d,1H), 7.37-7.56(m,5H), 7.59(td,1H), 7.64-7.70(m,2H), 7.72-7.74(m,1H), 7.74-7.76(m,2H).
ESI-Mass; 370 [M⁺+H]
[0538] The following compound was synthesized by the method similar to the method for Example 7.

50

Example 381.

3-(2-Cyanophenyl)-5-(2-pyridyl)-1-(2-nitrotoluen-4-yl)-1,2-dihydropyridin-2-one

- 55 [0539] ¹H-NMR (400MHz,CDCl₃) ; δ(ppm) 2.69(s,3H), 7.23-7.28(m,1H), 7.48(td,1H), 7.56-7.51(m,1H), 7.62(d,1H), 7.66(t,1H), 7.74-7.81(m,4H), 8.21(d,1H), 8.30(d,1H), 8.32(d,1H), 8.61(d,1H).

Example 382.

(382A) 3-(4-Chlorobenzenesulfinyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

5 (382B) 3-(4-Chlorobenzenesulfonyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0540] 6mg of 3-(4-chlorophenylthio)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 3ml of dichloromethane. Under ice-cooling, 3mg of m-chloroperbenzoic acid was added thereto, followed by stirring at the same temperature for 30 minutes. After stirring at room temperature for 5 hours, the mixture was diluted with 10ml of ethyl acetate, and washed with a 1N aqueous solution of sodium hydroxide. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 1.2mg of 3-(4-chlorobenzenesulfinyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one and 1.5mg of 3-(4-chlorobenzenesulfonyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one as the title compounds.

15 (382A)

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.23-7.29(m, 2H), 7.37-7.54(m, 6H), 7.72(dt, 1H), 7.79(td, 1H), 7.87(t, 1H), 7.89(t, 1H), 8.44(d, 1H), 8.57-8.60(m, 1H), 8.69(d, 1H).

ESI-Mass; 407 [M⁺+H]

(382B)

20 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.30(m, 2H), 7.37-7.40(m, 2H), 7.42-7.52(m, 4H), 7.67(dt, 1H), 7.80(td, 1H), 8.09(t, 1H), 8.11(t, 1H), 8.58(d, 1H), 8.60(ddd, 1H), 9.06(d, 1H).

ESI-Mass; 423 [M⁺+H]

[0541] The following compounds were synthesized by the methods similar to, or in accordance with, the method for Example 382.

25

Example 383.

(383A) 3-(2-Ethylsulfinylpyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

30 (383B) 3-(2-Ethylsulfonylpyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

[0542] (383A)

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.24(t, 3H), 2.96(dt, in), 3.21(dt, 1H), 7.23-7.27(m, 1H), 7.48-7.58(m, 5H), 7.60(d, 1H), 7.77(td, 1H), 8.03(d, 1H), 8.28(d, 1H), 8.38(d, 1H), 8.44(dd, 1H), 8.64(ddd, 1H), 9.04(d, 1H).

35 ESI-Mass; 402 [M⁺+H]

(383B)

¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.33(t, 3H), 3.44(q, 2H), 7.25-7.28(m, 1H), 7.49-7.62(m, 6H), 7.78(dd, 1H), 8.14(d, 1H), 8.31(d, 1H), 8.41(d, 1H), 8.51(dd, 1H), 8.64(ddd, 1H), 9.13(d, 1H).

ESI-Mass; 418 [M⁺+H]

40

Example 384.

3-(2-Ethylpyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

45 [0543] 13mg of 3-(2-chloropyridin-5-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of dimethylformamide, followed by the addition of 10mg of potassium carbonate and 2mg of tetrakis(triphenylphosphine) palladium. Under stirring at room temperature in nitrogen atmosphere, triethylborane (1.0M tetrahydrofuran solution) was added dropwise thereto, followed by heating under stirring at 100°C for 1 hour in nitrogen atmosphere. After the reaction mixture was cooled to room temperature, water was added thereto, and extracted with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 4mg of the title compound.

50 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.33(t, 3H), 2.87(q, 2H), 7.20-7.24(m, 2H), 7.44-7.60(m, 5H), 7.64-7.70(m, 1H), 7.75(td, 1H), 8.18(dd, 1H), 8.25(d, 1H), 8.26(d, 1H), 8.61(m, 1H), 8.84(d, 1H).

55

Example 385.

3-(2-Chlorophenyl)-5-(4-chlorophenylthio)-1-(3-pyridyl)-1,2-dihydropyridin-2-one

- 5 [0544] The title compound was synthesized by the method similar to the method for Example 188.
¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.23-7.50(m,8H), 7.52(d,1H), 7.55-7.58(m,1H), 7.72(d,1H), 7.86-7.93(m,1H), 8.66-8.76(m,2H).

Example 386.

10

3-(2-Cyanophenyl)-5-(1H-benzimidazol-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- [0545] The above compound was synthesized by the method similar to the method for Example 190.
¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.22-7.28(m,2H), 7.32-7.50(m,7H), 7.54-7.76(m, 4H), 8.20-8.21(m, 1H), 8.28-8.34(m, 1H).
 15 ESI-Mass; 389 [M⁺+H]

Example 387.

20

3-(2-Adamantyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0546] The above compound was synthesized by the method similar to the method for Example 178.
¹H-NMR (400MHz, CDCl₃); δ(ppm) 1.21-2.06(m, 12H), 2.48(s, 2H), 3.25(s, 1H), 7.18(ddd, 1H), 7.33-7.52(m, 5H), 7.54(d, 1H), 7.72(td, 1H), 8.09(d, 1H), 8.11-8.13(m, 1H), 8.60(ddd, 1H).

25

Example 388.

3-(2-Cyanophenyl)-5-(4-methyl-imidazo[4,5-b]pyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one

- 30 [0547] 3mg of 3-(2-cyanophenyl)-5-(1H-imidazo[4,5-c]pyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 3ml of acetone. To the mixture was added 2ml of methyl iodide, followed by stirring at room temperature overnight. The mixture was evaporated, and the residue was diluted with 1ml of water. To the mixture was added 20mg of sodium hydroxide, followed by stirring at room temperature for 4 hours. The reaction solution was extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous magnesium sulfate, and
 35 filtered. The filtrate was evaporated, and the residue was purified by silica gel chromatography (NH silica) (hexane/ethyl acetate system), to give 2mg of the title compound.
¹H-NMR(400MHz,CDCl₃); δ(ppm) 4.31(s,3H), 7.07(dd,1H), 7.43-7.61(m,7H), 7.64(td,1H), 7.72(dd,1H), 7.76(dd,1H), 8.09(d,1H), 8.71(d,1H), 8.73(d, 1H) .
 ESI-Mass; 404 [M⁺+H]

40

Example 389.

3-(2-Cyanophenyl)-1-phenyl-5-(3-phenyl-1,2,4-oxadiazol-5-yl)-1,2-dihydropyridin-2-one

- 45 [0548] 31mg of carboxylic acid, obtained by hydrolyzing 3-(2-cyanophenyl)-5-(methoxycarbonyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of dichloromethane, followed by the dropwise addition of a solution of 20mg of oxalyl chloride in dichloromethane under ice-cooling. A catalytic amount of dimethylformamide was added thereto, followed by stirring at room temperature for 1 hour in nitrogen atmosphere. The reaction solution was evaporated, and the residue was dissolved in dichloromethane. The mixture was added dropwise into a solution of 16mg of benzamidoxime and 0.05ml of triethylamine in toluene, under ice-cooling. After heating to room temperature, it was stirred in
 50 nitrogen atmosphere overnight. It was heated to 100°C for 1 hour, cooled to room temperature, and then washed with water. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and 28mg of the residue was dissolved in 10ml of toluene, followed by heating under reflux for 5 hours. After cooling to room temperature, the solvent was evaporated, to give 24mg of the title compound as white crystals.
 55 ¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.40-7.66(m, 9H), 7.68(dd, 2H), 7.80(dd, 1H), 8.12(dd, 2H), 8.32(dd, 1H), 8.52(dd, 1H).

Example 390.

3-(3-Phenyl-1,2,4-oxadiazol-5-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 5 [0549] The above compound was synthesized by the method similar to the method for Example 389.
¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.25-7.29(m,2H), 7.46-7.59(m,7H), 7.70(d, 1H), 7.81(td, 1H), 8.20-8.23(m, 2H), 8.59(d, 1H), 8.63(ddd, 1H), 9.14(d, 1H).

Example 391.

10

3-(2-Cyanothiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

- [0550] 22 mg of 3-(2-formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 20ml of ethanol. To the mixture were added 6.4mg of hydroxylamine hydrochloride and 10.1mg of sodium acetate, followed by heating at 80°C for 3 hours. After cooling the reaction mixture to room temperature, it was poured into a saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the resulting residue (25mg) obtained as an oxime compound was dissolved in 10ml of dimethylformamide, followed by adding 0.02ml of triethylamine. Under ice-cooling, 43mg of 1,1'-carbonyldiimidazole was added thereto, followed by stirring at 60°C for 1 hour. Then, it was cooled to room temperature, water was added thereto, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 15mg of the title compound as white crystals.
¹H-NMR (400MHz, CDCl₃); δ (ppm) 7.23(ddd, 1H), 7.46-7.58(m, 5H), 7.59(d,1H), 7.65(d, 1H), 7.77(td, 1H), 7.78(d, 1H), 8.38(d, 1H), 8.57(d, 1H), 8.59(ddd, 1H).
 ESI-Mass; 356 [M⁺+H]

Example 392.

30 3-[2-(5-Oxazolyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2 dihydropyridin-2-one

- [0551] 13mg of 3-(2-formylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one was dissolved in 10ml of methanol. To the mixture were added 11mg of tosylmethylisocyanide and 8mg of potassium carbonate, followed by heating under reflux overnight. After the reaction solution was cooled to room temperature, water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and brine, and then dried over anhydrous magnesium sulfate. It was filtered through NH silica gel and silica gel, and the filtrate was evaporated. The resulting precipitates were washed with ether and dried, to give 9mg of the title compound.
¹H-NMR (400MHz, CDCl₃); δ(ppm) 6.98(s, 1H), 7.20(ddd, 1H), 7.36-7.51(m, 7H), 7.54(dt, 2H), 7.72(ddd, 2H), 7.84(s, 1H), 8.11(d, 1H), 8.30(d, 1H), 8.59(ddd, 1H).

40

Example 393.

3-[2-(5-Oxazolyl)thiophen-3-yl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one

- 45 [0552] The title compound was synthesized by the method similar to the method for Example 392.
¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.14(s, 1H), 7.16-7.76(m, 10H), 7.82(s, 1H), 8.16(d, 1H), 8.29(d, 1H), 8.58(d, 1H).

Example 394.

50 3-(2-Cyanophenyl)-5-(2-pyridinecarbonyl)-1-phenyl-1,2-dihydropyridin-2-one

(394a) α-(2-Methoxypyridin-5-yl)-2-pyridinemethanol

- [0553] 50ml of a tetrahydrofuran solution containing 3.00g of 2-methoxy-5-bromopyridine was cooled to -78°C, followed by the dropwise addition of 10ml of n-butyl lithium (1.6M hexane solution). After the completion of the dropwise addition, 1.70g of picoline aldehyde was immediately added thereto, followed by stirring at -78°C for 1 hour, to return the mixture slowly to room temperature. To the mixture was added a saturated aqueous solution of ammonium chloride, and then it was extracted with ethyl acetate. The ethyl acetate layer was washed with water and brine, and then dried

over magnesium sulfate. The solvent was evaporated, and the resulting residue was purified by silica gel chromatography (ethyl acetate), to give 1.53g of the title compound as a pale yellow solid.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 3.93 (s, 3H), 5.87 (brs, 1H), 6.72(d, 1H), 7.24(d, 1H), 7.31-7.36(dd, 1H), 7.55-7.59 (dd, 1H), 7.74-7.80(dd, 1H), 8.21(d, 1H), 8.62(d, 1H).

(394b) 5-(2-Pyridinecarbonyl)-2-methoxypyridine

[0554] To a solution of 0.83g of α-(2-methoxypyridin-5-yl)-2-pyridinemethanol in 20ml of an acetone was added 1.70g of activated manganese dioxide, followed by vigorously stirring at room temperature for 30 minutes. The resulting precipitates were filtered off and washed with acetone. Then, the filtrate was concentrated, to give 0.80g of the title compound as a white solid.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 4.04(s, 3H), 6.84(dd, 1H), 7.48-7.54(ddd, 1H), 7.89-7.95(ddd, 1H), 8.09(d, 1H), 8.36-8.40(dd, 1H), 8.70-8.74(m, 1H), 9.09(d, 1H).

(394c) 5-(2-Pyridinecarbonyl)-1,2-dihydropyridin-2(1H)-one

[0555] 0.79g of 5-(2-pyridinecarbonyl)-2-methoxypyridine was dissolved in 5.0ml of 48% hydrobromic acid, and the mixture was stirred at 70°C for 30 minutes. It was ice-cooled, diluted with water and neutralized with potassium carbonate. The resulting precipitates were collected by filtration, washed with water and hexane, and dried, to give 0.51g of the title compound as a white powder.

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 6.45(d, 1H), 7.65-7.70(ddd, 1H), 7.95-8.00(dd, 1H), 8.05-8.20(m, 2H), 8.68-8.75 (m, 2H), 12.17(brs, 1H).

(394d) 5-(2-Pyridinecarbonyl)-3-bromo-1,2-dihydropyridin-2(1H)-one

[0556] To a solution of 0.23g of 5-(2-pyridinecarbonyl)-1,2-dihydropyridin-2(1H)-one in 2.0ml of dimethylformamide was added 0.21g of N-bromosuccinimide at room temperature, followed by stirring for 1 hour. The mixture was diluted with water, and the resulting precipitates were collected by filtration, washed with water and dried, to give 0.26g of the title compound as a pale yellow powder.

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.67-7.71(ddd, 1H), 7.99-8.03(ddd, 1H), 8.04-8.08(dd, 1H), 8.47(d, 1H), 8.73-8.75(m, 1H), 8.79(brs, 1H), 12.72(brs, 1H).

(394e) 5-(2-Pyridinecarbonyl)-1-phenyl-3-bromo-1,2-dihydropyridin-2-one

[0557] A suspension of 0.24g of 5-(2-pyridinecarbonyl)-3-bromo-1,2-dihydropyridin-2(1H)-one, 0.23g of phenylboronic acid, 0.30g of copper acetate and 1ml of triethylamine in 10ml of tetrahydrofuran was stirred at room temperature overnight. To the mixture were added concentrated aqueous ammonium (3ml), water (30ml) and ethyl acetate (100ml), to separate the organic layer. It was washed with water and brine, and then dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane), to give 0.21g of the title compound as a white powder.

¹H-NMR (400MHz, DMSO-d₆); δ(ppm) 7.50-7.60(m, 5H), 7.64-7.68(ddd, 1H), 8.02-8.09(m, 1H), 8.57(d, 1H), 8.66-8.70 (m, 1H), 9.00(d, 1H).

(394f) 3-(2-Cyanophenyl)-5-(2-pyridinecarbonyl)-1-phenyl-1,2-dihydropyridin-2-one

[0558] To a mixed liquid of 200mg of 5-(2-pyridinecarbonyl)-1-phenyl-3-bromo-1,2-dihydropyridin-2-one, 130mg of 2-(2-cyanophenyl)-1,3,2-dioxaborinate, 400mg of cesium carbonate and 6ml of dimethylformamide was added 60mg of tetrakis(triphenylphosphine) palladium, followed by stirring at 130°C for 5 hours in nitrogen atmosphere. After cooling to room temperature, ethyl acetate was added thereto. The extract was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane), to give 45mg of the title compound as a pale yellow powder.

¹H-NMR (400MHz, CDCl₃); δ(ppm) 7.40-7.58(m, 8H), 7.62-7.68(m, 1H), 7.75-7.78(d, 1H), 7.89-7.94(m, 1H), 8.11-8.15 (d, 1H), 8.47(d, 1H), 8.65-8.68(m, 1H), 9.16(d, 1H).

Example 395.

5-(2-Pyridinecarbonyl)-1-phenyl-3-phenyl-1,2-dihydropyridin-2-one

5 [0559] A mixed liquid of 10mg of 5-(2-pyridinecarbonyl)-1-phenyl-3-bromo-1,2-dihydropyridin-2-one, 10mg of phenylboronic acid, 40mg of cesium carbonate, 6mg of tetrakis(triphenyl)phosphine palladium and 1ml of dimethylformamide was stirred at 130°C for 2 hours in nitrogen atmosphere. After cooling to room temperature, ethyl acetate was added thereto. The extract was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane), to give 6mg of the title compound
10 as a pale yellow powder.
1H-NMR (400MHz, CDCl₃) ; δ(ppm) 7.32-7.58(m, 8H), 7.75-7.79(m, 2H), 7.88-7.94(ddd, 1H), 8.09-8.13(m, 1H), 8.42(d, 1H), 8.63-8.66(m, 1H), 9.01(d, 1H).

Example 396.

15

3-(2-Cyanophenyl)-5-(α-hydroxy-2-picolyl)-1-phenyl-1,2-dihydropyridin-2-one

[0560] To a solution of 25mg of 3-(2-cyanophenyl)-5-(2-pyridinecarbonyl)-1-phenyl-1,2-dihydropyridin-2-one in 5ml of methanol was added 2mg of sodium borohydride under ice-cooling. After 30 minutes, the mixture was diluted with a saturated aqueous solution of sodium hydrogen carbonate, followed by extracting with ethyl acetate. The ethyl acetate layer was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate), to give 15mg of the title compound as a pale yellow powder.
20 1H-NMR (400MHz, CDCl₃) ; δ(ppm) 5.72 (brs, 1H) , 7.32-7.72 (m, 13H) , 7.80-7.92 (m, 1H), 8.57-8.65 (m, 1H).

25

Example 397.

3-(2-Cyanophenyl)-5-(2-pyridin-2-yl-vinyl)-1-phenyl-1,2-dihydropyridin-2-one

30 [0561] A mixed liquid of 100mg of 3-(2-cyanophenyl)-1-phenyl-5-bromo-1,2-dihydropyridin-2-one, 100mg of 2-vinylpyridine, 6mg of palladium acetate, 17mg of tri-(o-tolyl)phosphine and 3ml of triethylamine was stirred at 130°C for 2 hours in nitrogen atmosphere. After cooling to room temperature, ethyl acetate was added thereto. The extract was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (ethyl acetate/hexane), to give 16mg of the title compound as a white powder.
35 1H-NMR (400MHz, CDCl₃) ; δ(ppm) 6.95-7.00(d, 1H), 7.16-7.21(m, 1H), 7.26-7.35(m, 1H), 7.44-7.60(m, 7H), 7.62-7.81(m, 5H), 8.03(d, 1H), 8.57-8.61(m, 1H).

Example 398.

40

3-[(2-Ethoxycarbonyl)vinylthiophen-3-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one

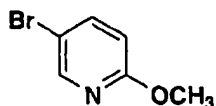
[0562] To a solution of 7.5mg of ethyl diethylphosphonoacetate in tetrahydrofuran was added 1.3mg of sodium hydride in nitrogen atmosphere under ice-cooling, followed by the dropwise addition of a solution of 10mg of 3-(2-formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one in tetrahydrofuran. After stirring the mixture at room temperature for 1 hour in nitrogen atmosphere, water was added thereto. Then, it was extracted with ethyl acetate. The organic layer was washed with brine, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel chromatography (hexane/ethyl acetate system), to give 4mg of the title compound.
45 1H-NMR (400MHz, CDCl₃) ; δ(ppm) 1.28(t, 3H), 4.21(q, 2H), 6.34(d, 1H), 7.19-7.23(m, 2H) 7.34-7.41(m, 2H), 7.43-7.56(m, 5H), 7.74(td, 1H), 7.88(d, 1H), 8.00(d, 1H), 8.30(d, 1H), 8.58-8.60(m, 1H).
50 ESI-Mass; 429 [M⁺+H]

55

Example 399.

5-Bromo-2-methoxypyridine

[0563]



[0564] 5-Dibromopyridine (200g) and 28% sodium methoxide methanol solution (1535g) were heated under reflux for 30 minutes, followed by cooling to room temperature. The mixture was partitioned between water (1.6L) and tert-butylmethyl ether (1.6L). The resulting organic layer was washed with brine (1L) for 3 times, and then dried over anhydrous MgSO_4 overnight. The dried organic layer was evaporated at 65°C , to give 160g (96%) of the title compound as a brown oil.

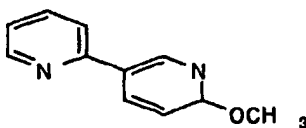
$^1\text{H-NMR}$ (400MHz, CDCl_3); $\delta(\text{ppm})$ 3.91 (3H, s), 6.66 (1H, d), 7.64 (1H, dd), 8.20 (1H, d).

MS: MH^+ 188, 190

Example 400.

6-Methoxy-3-pyridylboronic acid

[0565]



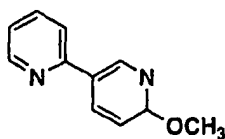
[0566] 5-Bromo-2-methoxypyridine (152g) was dissolved in tetrahydrofuran anhydride (1520mL) under stirring in nitrogen atmosphere, followed by cooling to -75.1°C as bulk temperature. Under cooling and stirring, 380mL of a 2.46mol/L butyl lithium solution was added dropwise thereto, followed by the dropwise addition of 192mL of trimethoxyborane. The cooling bath was removed 30 minutes after completion of the dropwise addition, and the mixture was stirred at room temperature overnight. On the next day, 1.5L of a 2mol/L aqueous solution of hydrochloric acid was added thereto, followed by stirring for 1.5 hours. of sodium hydroxide. It was then extracted with 1L of ethyl acetate, and the resulting aqueous layer was extracted again with 1L of ethyl acetate. The combined organic layer was washed twice with 1L of 10% saline water, dried over anhydrous magnesium sulfate, and then evaporated, to give 105g (88%) of the title compound as a slightly yellowish white solid.

$^1\text{H-NMR}$ (CDCl_3 ,400MHz):3.83(3H,s) , 6.74(1H,d), 7.98 (1H, dd) , 8.10 (2H, s), 8.50 (1H, s).

Example 401.

2-Methoxy-5-pyridin-2-yl-pyridine

[0567]



[0568] 6-Methoxy-3-pyridylboronic acid (105g), 2-bromopyridine (90g), palladium acetate (3.21g), triphenylphosphine (15g), potassium carbonate (237g), 1,2-dimethoxyethane (900mL) and water (900mL) were heated under reflux for 5 hours and 40 minutes under stirring. After cooling the reaction solution, ethyl acetate (1L) was added thereto to extract. The organic layer was washed with 1L of 10% aqueous solution of ammonium chloride, 1L of 10% aqueous ammonia and 1L of 10% saline, and then evaporated, to give 126g (87%) of the title compound.

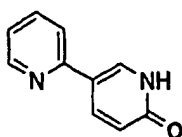
¹H-NMR (CDCl₃, 400MHz): 4.00(3H,s), 6.85(1H,d), 7.21-7.26(1H,m), 7.67(1H,d), 7.75(1H,dt), 8.25(1H,dd), 8.66-8.70(1H,m), 8.74(1H,d).

MS: MH⁺ 187

Example 402.

5-Pyridin-2-yl-2(1H)-pyridone

[0569]



[0570] A mixture of 2-methoxy-5-pyridin-2-yl-pyridine (550g) and a 4mol/L aqueous solution of hydrochloric acid (2.4L) was heated under reflux for 3 hours. After cooling the reaction solution, and washed with tert-butylmethyl ether (2.2L). To the aqueous layer was added 8mol/L aqueous solution of sodium hydroxide (1.1L) under cooling with ice-water, and then the mixture was washed twice with tert-butylmethyl ether (2.2L). Then, it was adjusted to pH 8 with concentrated hydrochloric acid (310ml) and 8mol/L aqueous solution of sodium hydroxide (100ml), followed by partitioning between 1-butanol (4.5L) and brine (1.8L). The aqueous layer was extracted again with 1-butanol (4.5L), and the combined organic layer was evaporated at 45-50°C. To the resulting residue was added tert-butylmethyl ether (2.2L), to give crystals. The resulting crystals were collected by filtration under reduced pressure and air-dried at 60°C. Then, water (1.6L) was added thereto to dissolve under heating. Then the mixture was water-cooled, and recrystallized. The resulting crystals were collected by filtration under reduced pressure and air-dried at 60°C, to give 188g (66%) of the title compound as grayish white crystals.

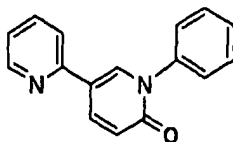
¹H-NMR (DMSO-d₆, 400MHz): 6.42 (1H, d), 7.19-7.26 (1H, m), 7.74-7.81 (2H, m), 8.11 (1H, d), 8.17 (1H, dd), 8.52-8.55 (1H, m).

MS: MH⁺ 173

Example 403.

1-Phenyl-5-pyridin-2-yl-2(1H)-pyridone

[0571]



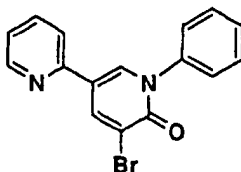
[0572] While stirring 5-Pyridin-2-yl-2(1H)-pyridone (185g), PhB(OH)₂ (261g), Cu(OAc)₂ (19.4g), pyridine (173ml) and DMF (1480ml) at room temperature, air was blown at 2.0L/minute therein, to initiate the reactions. Since 26% of the reactant remained unreacted 7 hours after the initiation of the reaction, flow of air was stopped to suspend the reactions. On the next day, air was blown into the solution to restart the reactions, and the reactant was consumed to 0.57% of the initial weight in 5.5 hours. The reaction solution was poured into ice-cooled 10% aqueous ammonia (7.5L), to give MA045. The resulting precipitates were collected by filtration under reduced pressure, and washed with water (3L).

The resulting crystals were suspended into 10% aqueous ammonia (3.6L) under stirring at room temperature for 1 hour. Then the crystals were collected by filtration under reduced pressure, and washed with water (2L). The resulting crystals were air-dried overnight, to give 187g (68%) of the title compound as brown crystals. ¹H-NMR (CDCl₃, 400MHz) : 6.77(1H,d), 7.19(1H,dd), 7.42-7.48(3H,m), 7.49-7.55 (3H, m), 7.72 (1H, dt), 8.04 (1H, dd), 8.21 (1H, d), 8.57-8.59 (1H, m).
MS: MH⁺ 249

Example 404.

3-Bromo-1-phenyl-5-pyridin-2-yl-2(1H)-pyridone

[0573]



[0574] 1-Phenyl-5-pyridin-2-yl-2(1H)-pyridone (186g), N-bromosuccinimide (141.7g) and N,N-dimethylformamide (900ml) were stirred at room temperature. After 2.5 hr, 6.45g of NBS was added thereto. After depletion of the reactant was confirmed, the reaction solution was poured into water (4.5L) under ice-cooling, followed by stirring in a cold-room (approximately 4°C) overnight. The resulting crystals were collected by filtration under reduced pressure, followed by dissolving in IPA (3.25L) and H₂O (650ml) under heating. After the complete dissolution was confirmed, the solution was left to cool gradually, and then ice-cooled. Then, the mixture was stirred in a cold-room overnight. The resulting crystals were collected by filtration under reduced pressure and air-dried at 60°C, to give 191g (81%) of the title compound.

¹H-NMR (CDCl₃, 400MHz): 7.19-7.24 (1H, m), 7.42-5.56 (6H, m), 7.74 (1H, dt), 8.19 (1H, d), 8.51 (1H, d), 8.58-8.61 (1H, m).

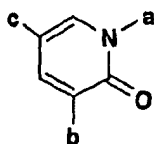
MS: MH⁺ 327, 329









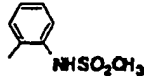








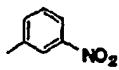


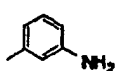


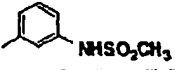


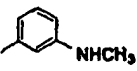


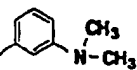


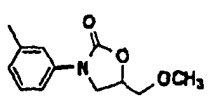


[0575] Among the above Examples, the particularly preferable compounds include 3-(2-cyanophenyl)-5-(2-methylsulfonylaminophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-dimethylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-[3-(5-methoxymethyl-2-oxazolidinon-3-yl)-phenyl]-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminocarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyano-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetylaminomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylaminomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-acetoxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylthiophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methylsulfonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-formylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-diethylaminomethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-hydroxymethylthiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-benzyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-phenyl-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1,5-diphenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-methoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3,4-dimethoxyphenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(thiophen-3-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-fluorophenyl)-1-phenyl-1,2-dihydropyridin-2-

one; 3-(2-cyanophenyl)-5-(thiophen-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3-furfuryl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-furfuryl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-methoxycarbonylphenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-fluorophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(4-methoxy-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-(3-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-fluorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-chlorophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-tolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-trifluoromethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-furfuryl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-tolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-trifluoromethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-methoxypyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(pyrimidin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-benzoyloxymethylpyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-ethylthiopyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxypyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-chloropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-fluoropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-methoxyphenyl)-1,2-dihydropyridin-2-one; 3-phenyl-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(thiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2,6-dimethylphenyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-fluoro-3-pyridyl)-5-(2-pyridyl)-1-(3-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-hydroxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(3-dimethylaminopropoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-hydroxymethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(4-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-cyanomethylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(6-diethylaminomethyl-2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-hydroxypyridin-6-yl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-(2-aminobenzothiazol-6-yl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-benzyl-1,2,3,6-tetrahydropyridin-5-yl)-1,2-dihydropyridin-2-one; 3-[2-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(6-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(5-methylpyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(3-hydroxypyridin-2-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-phenyl-5-(2-thiazoyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-methoxypyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one; 1-(4-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-(3-aminophenyl)-3-(2-cyanophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-aminotoluen-4-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(dimethylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(piperidinoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(pyrrolidinoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(diisopropylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(4-piperidinobutyl-1-oxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(4-nitrophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-phenyl-5-(2-pyridyl)-3-(2-thiazoyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-fluoropyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-nitrophenyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-naphthyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-naphthyl)-1,2-dihydropyridin-2-one; 5-(2-aminopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 5-(2-bromopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-morpholinopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-hydroxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(4-piperidyloxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-[3-(N-acetyl piperidin-4-yloxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(1-methanesulfonyl)piperidin-4-yl-oxy]phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-[3-(N-methylpiperidin-4-yloxy)phenyl]-3-(2-cy-



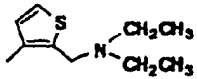


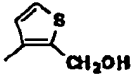



































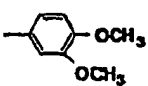



EP 1 300 396 A1


















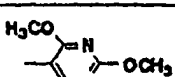


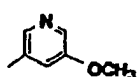





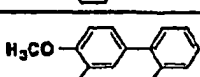






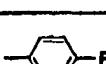






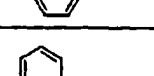


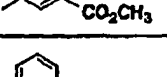

anophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(6-chloro-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-nitrotoluen-4-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)thiophen-3-yl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; and 3-[(2-ethoxycarbonyl)vinylthiophen-3-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one.


























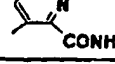


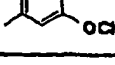


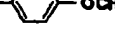










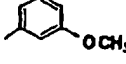





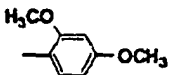





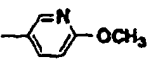







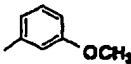





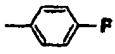





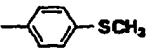



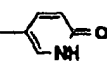

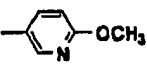





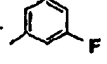



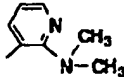

Example	a	b	c
1			
2			
3			
4			
6	H		
7			
8			
9			
10			
11			
12			
13			

Example	a	b	c
14			
15			
16			
17			
18			
19			
20			
21			
22			
23			
24			
25			
26			
27			
28			







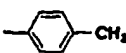


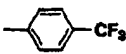


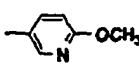








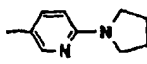


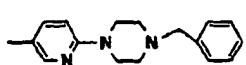





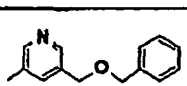


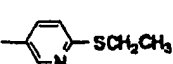





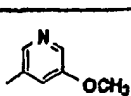


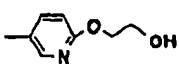


Example	a	b	c
29			
30			
32			
33			
34			
35			
36			
37			
38			
39			
40			
41			
42			
43			
44			

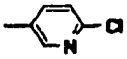


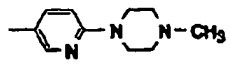


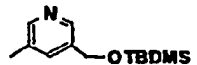


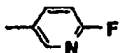


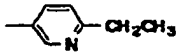





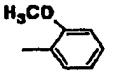












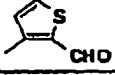


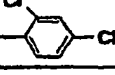







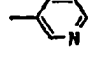
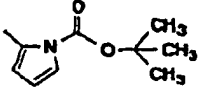

Example	a	b	c
4 5			
4 6			
4 7			
4 8			
4 9			
5 0			
5 1			
5 2			
5 3			
5 4			
5 5			
5 6			
5 7			
5 8			
5 9			


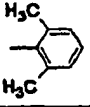


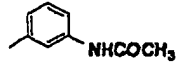





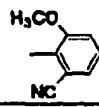





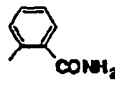




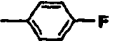


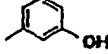





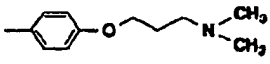


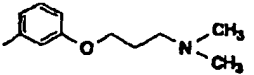



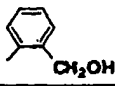

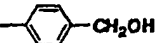


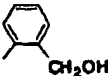


Example	a	b	c
6 0			
6 1			
6 2			
6 3			
6 4			
6 5			
6 6			
6 7			
6 8			
6 9			
7 0			
7 1			
7 2			
7 3			
7 4			

Example	a	b	c
7 5			
7 6			
7 7			
7 8			
7 9			
8 0			
8 1			
8 2			
8 3			
8 4			
8 5			
8 6			
8 7			
8 8			
8 9			




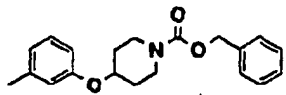






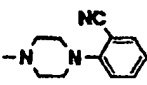









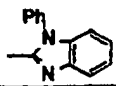


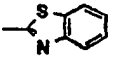


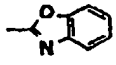


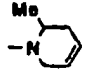




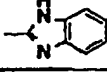








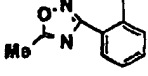

	a	b	c
9 0			
9 1			
9 2			
9 3			
9 4			
9 5			
9 6			
9 7			
9 8			
9 9			
1 0 0			
1 0 1			
1 0 2			
1 0 3			
1 0 4			



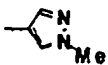


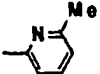


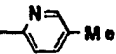


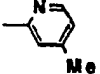








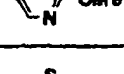

















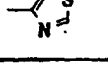






Example	a	b	c
105			
106			
107			
108			
109			
110			
111			
112			
113			
114			
115			
116			
117			
118			
119			






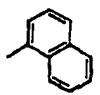


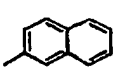


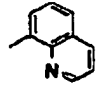





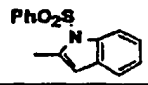
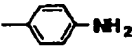







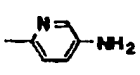
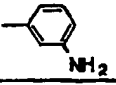






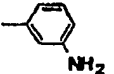


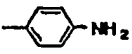

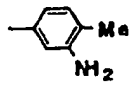




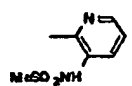
Example	a	b	c
1 2 0			
1 2 1			
1 2 2			
1 2 3			
1 2 4			
1 2 5			
1 2 6			
1 2 7			
1 2 8			
1 2 9			
1 3 0			
1 3 1			
1 3 2			
1 3 3			
1 3 4			


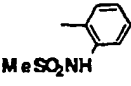


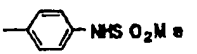


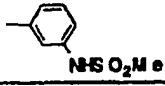



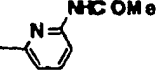

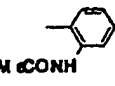


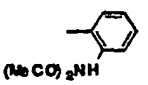


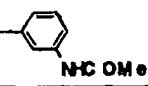


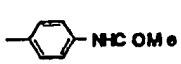


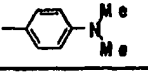



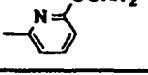


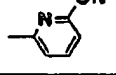




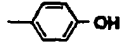

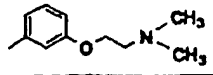


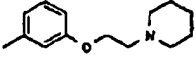


Example	a	b	c
1 3 5			
1 3 6			
1 3 7			
1 3 8			
1 3 9			
1 4 0			
1 4 1			
1 4 2			
1 4 3			
1 4 4			
1 4 5			
1 4 6			
1 4 7			
1 4 8			
1 4 9			

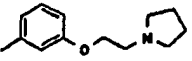


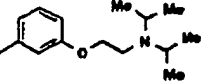


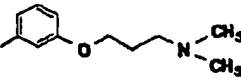


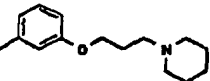


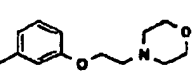


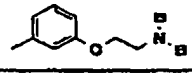



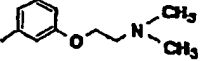


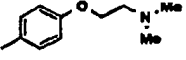




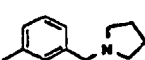


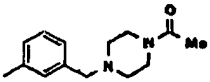














Example	a	b	c
1 5 0			
1 5 1			
1 5 2			
1 5 3			
1 5 4			
1 5 5			
1 5 6			
1 5 7			
1 5 9			
1 6 0			
1 6 2			
1 6 3			
1 6 4			
1 6 5			
1 6 6			














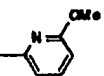
















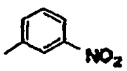














Example	a	b	c
171			
172			
173			
177			
178			
180			
182			
183			
184			
186			
189			
190			
191			
192			
193			





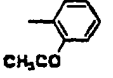


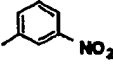


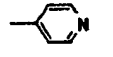


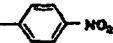

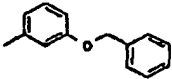
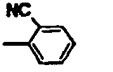

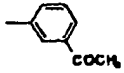
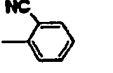


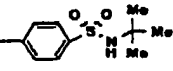


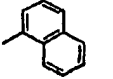


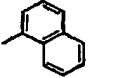


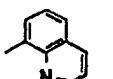


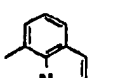


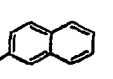


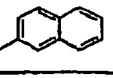


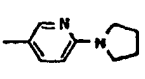

Example	a	b	c
194			
195			
196			
197			
198			
199			
200			
201			
202			
203			
204			
205			
206			
207			
208			


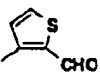


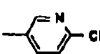


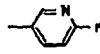


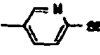

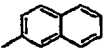


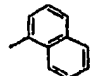


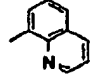



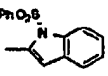












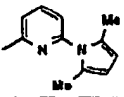





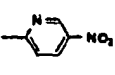



Example	a	b	c
2 0 9			
2 1 0			
2 1 1			
2 1 2			
2 1 3			
2 1 4			
2 1 5			
2 1 6			
2 1 7			
2 1 8			
2 1 9			
2 2 0			
2 2 1			
2 2 2			
2 2 5			



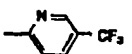


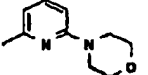





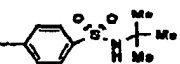

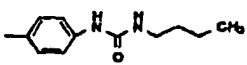

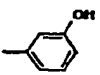









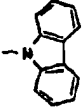





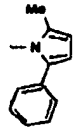


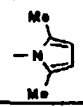

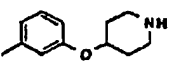


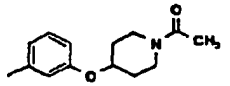


Example	a	b	c
2 2 6			
2 2 7			
2 2 8			
2 2 9			
2 3 0			
2 3 1			
2 3 2			
2 3 3			
2 3 4			
2 3 5			
2 3 6			
2 3 7			
2 3 8			
2 3 9			
2 4 0			

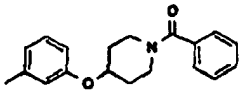


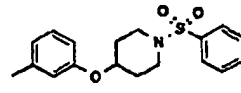


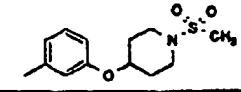


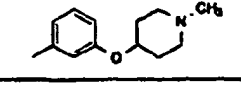


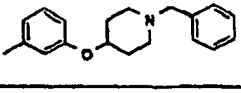



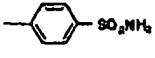



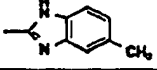


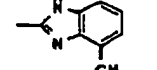


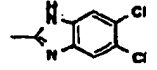

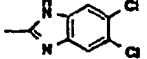


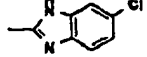


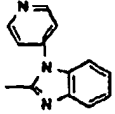


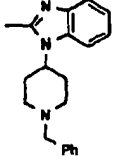

Example	a	b	c
2 4 1			
2 4 2			
2 4 3			
2 4 4			
2 4 5			
2 4 6			
2 4 7			
2 4 8			
2 4 9			
2 5 0			
2 5 1			
2 5 2			
2 5 3			
2 5 4			
2 5 5			



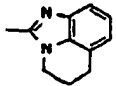

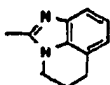


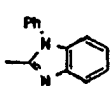



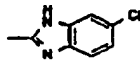


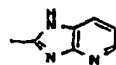

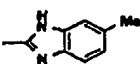


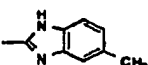



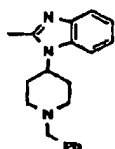


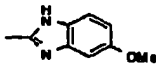

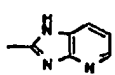


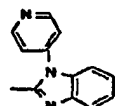



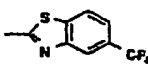

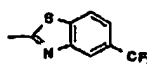


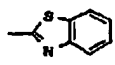

Example	a	b	c
2 5 6			
2 5 7			
2 5 8			
2 5 9			
2 6 0			
2 6 1			
2 6 2			
2 6 3			
2 6 4			
2 6 5			
2 6 6			
2 6 7			
2 6 8			
2 6 9			
2 7 0			


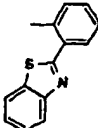
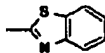

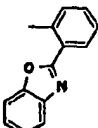
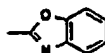





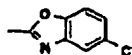

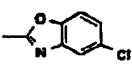


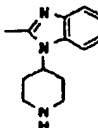



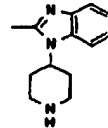


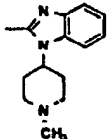









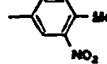


Example	a	b	c
2 7 1			
2 7 2			
2 7 3			
2 7 4			
2 7 5			
2 7 6			
2 7 7			
2 7 8			
2 7 9			
2 8 0			
2 8 1			
2 8 2			
2 8 3			
2 8 4			
2 8 5			


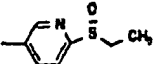


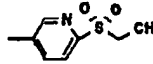


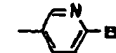



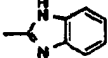





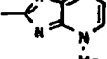


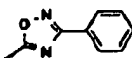

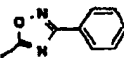





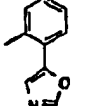


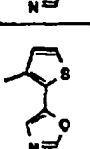


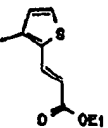

Example	a	b	c
2 8 6			
2 8 7			
2 8 8			
2 8 9			
2 9 0			
2 9 1			
2 9 2			
2 9 3			
2 9 4			
2 9 5			
2 9 6			
2 9 7			
2 9 8			
2 9 9			
3 0 0			

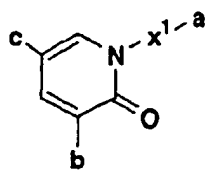
Example	a	b	c
3 0 1			
3 0 2			
3 0 3			
3 0 4			
3 0 8			
3 1 5			
3 2 0			
3 2 4			
3 2 5			
3 2 6			
3 2 7			
3 2 8			
3 3 0			
3 3 3			

Example	a	b	c
3 3 4			
3 3 7			
3 3 8			
3 4 1			
3 4 2			
3 4 3			
3 5 1			
3 5 2			
3 5 3			
3 5 4			
3 5 5			
3 5 6			
3 5 7			

Example	a	b	c
3 5 8			
3 5 9			
3 6 0			
3 6 1			
3 6 2			
3 6 3			
3 6 4			
3 6 5			
3 6 6			
3 6 7			
3 6 8			
3 6 9			
3 7 0			
3 7 1			

Example	a	b	c
3 7 2			
3 7 3			
3 7 4			
3 7 5			
3 7 6			
3 7 7			
3 7 8-A)			
3 7 8-B)			
3 7 9-A)			
3 7 9-B)			
3 8 0			
3 8 1			

Example	a	b	c
3 8 3 -A)			
3 8 3 -B)			
3 8 4			
3 8 6			
3 8 7			
3 8 8			
3 8 9			
3 9 0			
3 9 1			
3 9 2			
3 9 3			
3 9 8			



5

10

15

20

25

30














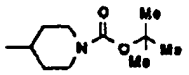


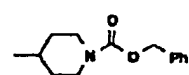


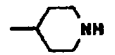


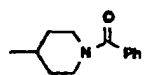


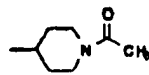


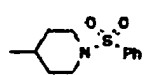


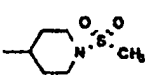


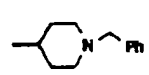


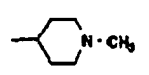


35

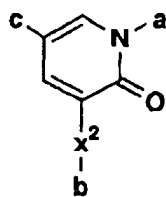
40

45




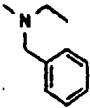









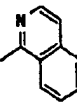











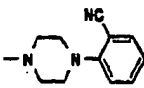











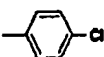



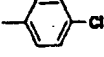


50

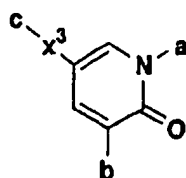
55

























































Example	a	b	c	X ¹
3 1				-CH ₂ -
1 5 8				-CH ₂ CH ₂ -
3 1 6				
3 1 7				-CH ₂ -
3 1 8				-CH ₂ -
3 1 9				-CH ₂ -
3 2 9				-CH ₂ -
3 3 1				-CH ₂ -
3 3 2				-CH ₂ -
3 3 5				-CH ₂ -
3 3 6				-CH ₂ -
3 3 9				-CH ₂ -
3 4 0				-CH ₂ -

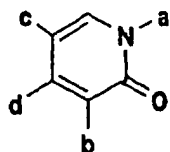








Example	a	b	c	x2
1 6 1				
1 6 8				
1 6 9				
1 7 0				
1 7 4				
1 7 5				
1 7 6				
1 7 9				
1 8 7				
1 8 8				
2 2 3				
3 0 6				
3 1 0				
3 1 1				
3 1 2				

Example	a	b	c	x2
3 1 4				
3 2 1				
3 2 2				
3 2 3				
3 4 4				
3 4 6				
3 4 7				
3 4 8				
3 4 9				
3 8 2-A				
3 8 2-B				



Example	a	b	c	x3
1 8 1				
1 8 5				
2 2 4				
3 0 7				
3 0 9				
3 1 3				
3 4 5				
3 5 0-A				
3 5 0-B				
3 8 5				
3 9 4				
3 9 5				
3 9 6				
3 9 7				



Example	a	b	c	d
1 6 7				CH ₃ -
3 0 5				CH ₃ -

Test Example 1.

[0576] The suppressing action of the compounds of the present invention to calcium influx into nerve cells induced by AMPA was investigated using the primary culture system of nerve cells of cerebral cortex of embryo of rat.

Culturing Conditions:

[0577] Cerebral cortex was cut out from the brain of rat of gestational 18 days and treated with trypsin and DNase to disperse the cells. The cells were flown by MEM containing 10% of serum, sown in a culture bottle and astrocytes were proliferated. The astrocytes were re-dispersed by trypsin and sown in a 96-well plate. After incubation for one week, it was confirmed that the astrocytes covered all over the bottom and then the nerve cells of cerebral cortex which was dispersed by the above method were sown thereupon. After incubation for 24 hours, the medium was changed, the incubation was carried out for one week and, after that, the medium was changed to that containing 1 μ M of MK-801. Nerve cells which were incubated for not shorter than 8 to 10 days were used.

Suppressing Action to Calcium Influx into Nerve Cells Induced by AMPA

[0578] Calcium influx into the cells was measured using Fura2-AM which was a calcium-sensitive fluorescent dye. It was treated in a medium containing Fura2-AM for 1 hour, incorporated into the cells, exchanged to a Tyrode solution containing 1 μ M MK-801 and stimulation was carried out using 2 μ M AMPA. Change in the amount of calcium flown into the cells were measured as the change in the fluorescent intensity at the exciting wave length of 340/380 nm. Effect of the test compound was evaluated using the reaction resulted in the AMPA added to a Tyrode solution containing no compound as a control. Results are shown in Tables 1 to 3.

[0579] GYKI 52446 (Le Peillet, et al., Brain Res., 571, 115, 1992) was used as a control compound. IC₅₀ of GYKI 52466 was 9.02 μ M.

Test Example 2.Anticonvulsant Action Induced by AMPA

[0580] A test compound was suspended in a 0.5% methyl cellulose solution or in sesame oil and was orally administered (25 mg/kg) to male mice of ddy strain. After 30 minutes or 1 hour from the oral administration, AMPA was continuously injected (2 nmole/5 μ l/minute/mouse) into lateral ventricle to induce the convulsions. The effect was judged by a time-extending action until the convulsion takes place by a continuous injection of AMPA.

Results

[0581] The compound represented by the above formula (I) according to the present invention showed an excellent anticonvulsant action. For example, the compounds of Examples 4, 7, 9, 12, 16, 32, 41, 47, 57, 61, 76, 78, 91, 126, 128, 137, 139, 164, 199, 261, 262, 264, 270 and 298 showed a significant anticonvulsant action.

Test example 3

Occlusion model of midcerebral arteries

5 [0582] The usefulness of the compound related to the present invention in the remedy of cerebral vascular accident acute stage was confirmed by the test below. Namely, the cerebral bloodstream of midcerebral arteries was blocked by inserting a nylon suture thread of 4-0 specification whose edge was crashed with flame, by 17mm from the branch of internal carotid artery, through internal carotid artery from the external carotid artery of a male Sprange Dawley rat, and cerebral infarction was prepared (Zea Longa et al., Stroke 20:84-91, 1989). The size of the cerebral infarction was evaluated by preparing the intersection slice of brain having a thickness of 2mm and measuring the area of a portion which was not stained by TTC staining. The effect of the tested substance was carried out in this model by comparing the infarction nidus size between a group treated with a solvent and a group treated with the tested substance.

10 [0583] As a result, the compound related to the present invention revealed an excellent effect as the therapeutic agent of cerebral vascular accident acute stage.

15

Test Example 4

Antimethamphetamine effect

20 [0584] (S)-(+)-N, α -dimethylphenethylamine (hereinafter, referred to as "methamphetamine") was dosed intraperitoneal injection to a rat or mouse to which the tested compound was dosed, and a quantity of active movement was measured using an active movement measuring apparatus (SCANET SV-10; manufactured by TOYO Sangyo Co., Ltd.). The activity as the therapeutic agent of schizophrenia was evaluated using the hyperdynamic effect control of active movement caused by methamphetamine as an index (K.E.Vanover, Psychopharmacology 136: 123-131, 1998).

25 The effect of the tested substance was confirmed by the control effect of a quantity of active movement accentuation in comparison with the group dosed with a solvent.

[0585] As a result, the compound related to the present invention revealed an excellent methamphetamine effect.

Test Example 5

30

Rigidity model of intercaruncle ablatio provocative muscle

[0586] An animal model in which the myotony of anteroposterior limbs was provoked was prepared by electrically freezing between the upper cumulus and the lower cumulus of a rat. Myorelaxation effect was evaluated based on the effect of controlling the increase of muscle discharge which is generated when the posterior limbs in this model are moved back and forth. The effect of the tested substance was confirmed by the changes of muscle discharge amount before dosing the tested substance and muscle discharge amount after dosing it.

[0587] The compound related to the present invention revealed an excellent myorelaxation effect.

40 Test Example 6

Light dark test

45 [0588] A mouse is put in a dark box which is composed of two light and dark boxes which are linked by a tunnel, and items below were recorded concerning the behavior of the mouse for 5 minutes after that.

1. A time for remaining in the light and dark boxes.
2. Times by which the mouse went and came back between the light box and the dark box.
3. Times by which the mouse went until the entrance of the light box.

50

[0589] The antianxiety effect of the tested compound was detected as the elongation of the time remaining in the light and dark boxes, the increase of times by which the mouse went and came back between the light box and the dark box, and the increase of times by which the mouse went until the entrance of the light box, for the group dosed with a solvent (Hascoet M., Bourin M., Pham. Biochem. Behav. 60: 645-653, 1998).

55 [0590] According to the present test, it was confirmed that the compound related to the present invention has an excellent antianxiety effect.

Test example 7

Destruction model of 6-hydroxydopamine-inductive nigrostriaton

5 [0591] 10mg/kg of L-Dihydroxyphenylalanine (L-DOPA) (twice per day) was dosed every day in the abdomen of a rat whose one side of nigra neurocyte was destroyed by injecting 6-hydroxydopamine (6-OHDA) into nigra, therefore the increase of rotational motion to the reverse side of encephalopathy was provoked (C.Marin et al, Synapse 36(4): 267-274, 2000). After the solvent or the tested compound was dosed to the rat, influence on the provoked rotational motion was studied. The tested compound delayed the time until primitive rotational motion shows the maximum value
10 after dosing L-DOPA, and increased the time of showing rotation which is a half or more of the maximum rotational number.

Test example 8

15 Acetic acid writhing method

[0592] Anguishing condition under which the lower half of rat's body was twisted, its abdomen was dented and its hind legs were extended was provoked by injecting 0.6% acetic acid saline in the abdomen of the rats. After the tested compound and the solvent were dosed, the acetic acid saline was injected in the abdomen, and analgesic effect was
20 evaluated by comparing the times of these abnormal actions within an observation time (5 to 15 minutes after the dose of acetic acid) which occur after the dosing (Basic Pharmacology Experiment, edited by Kazuhiko Kubota, pages 45-47, Nankoh-do).

[0593] As a result, it could be confirmed that the compound related to the present invention controls the times of the abnormal actions significantly and has an excellent analgesic effect.

25

Test example 9

Vomiting model induced by cisplatin

30 [0594] A catheter for venoclysis was buried in a ferret, and the rat was postoperatively recovered. Then, vomiting reaction was provoked by injecting 10mg/kg of cisdiaminedichloroplatinum (cisplatin) (A.Fink-Jensen et al., Neuroscience Letters 137: 173-177, 1992). Cisplatin (10mg/kg) was injected a ferret which was preliminarily treated with the tested compound or the solvent, then the ferret was put in an observation cage, and the time (latent time) and times until the rhythmical contraction of abdomen (defined as vomiting) occurs during the observation period of 240 minutes
35 were measured.

[0595] As a result, the compound related to the present invention reduced the latent time and the vomiting times significantly.

40 Test example 10

Experimental autoimmune encephalomyelitis model

[0596] Female Lewis rats (205 ± 10 g) obtained from Charles River, Kent UK, were housed in pairs under environmentally controlled conditions (6:00a.m.-6:00p.m. light/dark cycle; 22-24°C; 45-55% humidity) and allowed free access
45 to food and water. Experimental groups consisted of 9-12 animals. Rats were immunised in each hind foot with 20-50 µl of inoculum containing 50 µg guinea pig myelin basic protein (MBP; final concentration 2 mg/ml), emulsified in Freund's complete adjuvant (CFA; Sigma, UK) containing Mycobacterium tuberculosis H37Ra (final concentration 5.5 mg/ml; Difco Laboratories, UK). Animals were weighed and monitored daily and clinical disease scored as (0) no clinical signs; (1) flaccid tail and weight loss; (2) hind limb hypotonia with further weight loss; (3) complete hind limb paralysis;
50 (4) paraplegia and (5) death. In addition, intermediate scores were assigned to animals which showed a loss of tonicity in the distal half of the tail (score = 0.5), paralysis of one hind limb (score = 2.5) or complete hind limb paralysis with forelimb weakness (score = 3.5). During the period of compound administration (10-16 days post immunisation; dpi) animals were scored 15h after injection of vehicle or compound to avoid any acute effect of treatment on disease score. Compounds were dissolved/suspended in 0.5% methyl cellulose using a hand held Polytron homogeniser (PT1200;
55 2 min). Rats were dosed p.o. with either methyl cellulose vehicle (2.5 ml/kg) or compound at 5, 10 and 20 mg/kg. Results: the compound of the invention is improved in view of experimental autoimmune encephalomyelitis. The compounds of Examples 7, 32, 76, 139, 164, 261, 262 and 264 are for example provided with a superior effect to the vehicle-administered group.

EP 1 300 396 A1

Table 1

	Example	I C ₅₀ (μM)	Example	I C ₅₀ (μM)	Example	I C ₅₀ (μM)
5	1	0.8	42	0.2	92	0.05
	2	1.8	43	0.5	93	1.9
	3	0.3	44	0.3	94	1.5
	4	0.1	45	0.2	95	0.3
10	5	0.6	46	0.4	96	0.06
	6	9.3	47	0.6	97	0.4
	7	0.1	48	0.04	98	0.6
15	8	0.1	49	0.2	99	0.1
	9	0.03	52	1.1	100	0.4
	10	0.05	55	0.8	101	0.2
	11	0.06	56	3.2	102	0.02
20	12	0.1	57	0.2	103	0.03
	13	0.2	58	0.1	104	0.2
	14	0.1	60	1.7	105	0.03
25	15	0.05	61	0.2	106	0.07
	16	0.1	62	3.1	107	0.07
	17	0.7	63	1.1	108	0.03
30	18	0.02	64	2.8	109	0.01
	19	0.08	65	0.6	110	2.0
	20	0.04	66	2.4	111	0.4
	21	0.03	67	6.5	112	0.6
35	22	0.06	69	0.9	113	1.2
	23	0.2	70	3.1	114	0.6
	24	0.2	71	0.05	115	0.06
40	25	0.03	72	0.7	116	0.2
	26	0.02	73	1.2	117	0.4
	27	0.05	74	0.2	118	0.1
	28	0.2	76	0.1	119	1.7
45	29	0.1	77	0.02	120	0.2
	30	0.04	78	1.4	121	0.6
	31	0.1	79	2.6	123	0.2
50	32	0.1	80	0.3	124	0.7
	33	0.7	81	2.7	126	0.3
	34	3.7	82	0.8	127	0.4
	35	3.1	84	0.9	128	0.07
55	36	1.1	86	1.9	129	2.6
	37	0.7	87	1.2	130	0.9

EP 1 300 396 A1

Table 1 (continued)

Example	I C ₅₀ (μM)	Example	I C ₅₀ (μM)	Example	I C ₅₀ (μM)
38	6.3	88	0.3	131	3.7
39	0.3	90	0.7	132	3.1
41	0.08	91	0.05	133	0.3

Table 2

Example	I C ₅₀ (μM)	Example	I C ₅₀ (μM)	Example	I C ₅₀ (μM)
135	0.04	199	0.7	251	0.9
137	0.05	200	2.0	252	0.3
139	0.3	201	0.2	253	4.7
140	6.6	202	0.7	255	0.5
141	0.7	204	1.6	256	1.2
142	2.2	206	0.5	257	3.7
143	0.1	209	7.0	259	2.0
144	0.01	210	5.2	260	2.7
146	0.2	211	3.6	261	0.08
147	1.6	215	0.1	262	0.3
148	0.8	216	2.4	263	1.0
149	0.1	217	1.3	264	0.05
150	0.3	218	0.1	265	0.7
151	0.3	219	3.7	266	0.1
152	4.0	220	0.6	267	1.0
154	5.0	221	7.1	268	4.2
157	0.5	222	0.2	269	1.9
159	1.6	226	9.5	270	0.14
163	8.2	227	1.8	272	3.3
164	0.08	228	2.7	275	6.1
165	0.4	229	4.2	276	1.9
166	0.3	230	4.0	277	0.6
171	2.3	232	4.3	278	2.8
173	4.2	234	0.9	279	3.7
174	3.3	235	4.4	280	1.3
176	5.4	236	0.6	282	9.0
178	2.0	237	1.5	284	2.8
180	0.5	238	0.6	285	7.2
182	6.0	239	0.3	286	0.3
184	2.3	240	0.1	287	5.6
185	1.7	241	0.4	288	1.2
187	6.1	242	0.5	290	0.2

EP 1 300 396 A1

Table 2 (continued)

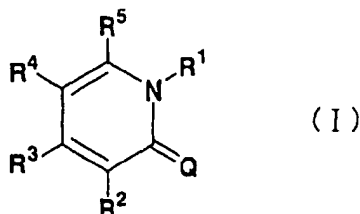
Example	IC ₅₀ (μM)	Example	IC ₅₀ (μM)	Example	IC ₅₀ (μM)
188	8.5	243	1.2	291	0.14
190	0.6	244	1.8	292	3.3
192	1.1	245	1.2	293	3.3
193	0.4	246	1.1	294	0.6
195	0.2	247	3.6	297	4.2
196	0.3	248	3.4	298	0.3
197	2.9	249	0.3	299	4.4
198	0.3	250	0.9	300	0.3

Table 3

Example	IC ₅₀ (μM)	Example	IC ₅₀ (μM)	Example	IC ₅₀ (μM)
302	0.3	334	0.6	367	0.6
303	0.9	337	0.7	371	0.6
307	2.0	338	0.4	379-B	6.4
308	1.6	341	0.2	381	0.4
309	4.1	342	1.3	382-B	2.3
313	5.9	342	3.2	385	1.1
314	4.6	344	4.7	386	3.5
315	0.08	346	3.7	387	7.0
316	2.1	351	3.3	388	2.9
317	0.6	352	1.6	390	1.0
318	3.1	354	1.5	391	0.1
319	2.0	355	0.2	392	0.1
320	2.3	356	2.1	393	0.3
321	4.0	358	1.4	394	1.4
326	0.9	359	2.3	395	0.9
327	8.0	360	3.1	398	0.2
330	0.4	362	3.7		
333	0.3	365	2.7		

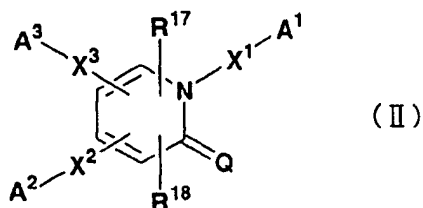
Claims

1. A compound represented by the following formula, a salt thereof or hydrates thereof.



In the formula, Q indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or a group represented by the formula -X-A (wherein X indicates a single bond, an optionally substituted C₁₋₆ alkylene group, an optionally substituted C₂₋₆ alkenylene group, an optionally substituted C₂₋₆ alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicate hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q indicates an integer of 0, 1 or 2 independently); and A indicates a C₃₋₈ cycloalkyl group, a C₃₋₈ cycloalkenyl group, a 5 to 14 membered non-aromatic heterocyclic group, a C₆₋₁₄ aromatic hydrocarbocyclic group, or a 5 to 14 membered aromatic heterocyclic group which may be substituted respectively, provided that 3 groups among R¹, R², R³, R⁴ and R⁵ are always the same as or different from each other and each indicates -X-A; and the residual 2 groups always indicate hydrogen atom, a halogen atom or a C₁₋₆ alkyl group), provided that in the above-mentioned definition, the cases where (1) Q is O; R¹ and R⁵ are hydrogen atoms; and R², R³ and R⁴ are phenyl groups, (2) Q is O; R¹ and R⁴ are hydrogen atoms; and R², R³ and R⁵ are phenyl groups, and (3) Q is O; R¹ and R² are hydrogen atoms; and R³, R⁴ and R⁵ are phenyl groups, are excluded.

2. The compound according to Claim 1, a salt thereof or hydrates thereof, which is represented by the formula:



wherein Q indicates NH, O or S; X¹, X² and X³ are the same as or different from each other and each indicates a single bond, an optionally substituted C₁₋₆ alkylene group, an optionally substituted C₂₋₆ alkenylene group, an optionally substituted C₂₋₆ alkynylene group, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicate hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q are independent of each other and each indicates an integer of 0, 1 or 2); A¹, A² and A³ are the same as or different from each other and each indicates an optionally substituted C₃₋₈ cycloalkyl group, C₃₋₈ cycloalkenyl group, 5 to 14-membered non-aromatic heterocyclic group, C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group; and R¹⁷ and R¹⁸ are the same as or different from each other and each indicates hydrogen atom, a halogen atom or a C₁₋₆ alkyl group.

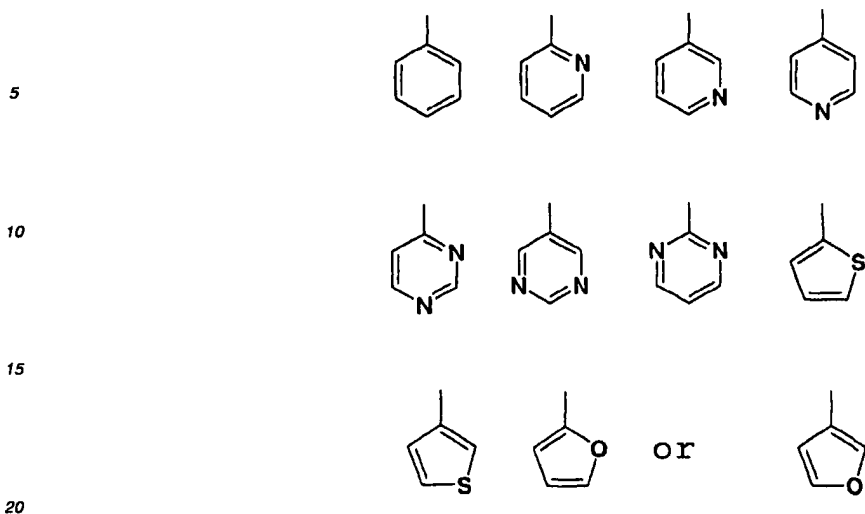
3. The compound according to claim 2, a salt thereof or hydrates thereof, wherein X¹, X² and X³ are (1) single bond, (2) a C₁₋₆ alkylene group, a C₂₋₆ alkenylene group or a C₂₋₆ alkynylene group which may be optionally substituted respectively with one or more groups selected from the following substituent group a, (3) -O-, (4) -S-, (5) -CO-, (6) -SO-, (7) -SO₂-, (8) -N(R⁶)-, (9) -N(R⁷)-CO-, (10) -CO-N(R⁸)-, (11) -N(R⁹)-CH₂-, (12) -CH₂-N(R¹⁰)-, (13) -CH₂-CO-, (14) -CO-CH₂-, (15) -N(R¹¹)-S(O)_m-, (16) -S(O)_n-N(R¹²)-, (17) -CH₂-S(O)_p-, (18) -S(O)_q-CH₂-, (19) -CH₂-O-, (20) -O-CH₂-, (21) -N(R¹³)-CO-N(R¹⁴)- or (22) -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶, m, n, p and q have the same meanings as defined in the above Claim 1); and A¹, A² and A³ are a C₃₋₈ cycloalkyl group, a C₃₋₈ cycloalkenyl group, a 5- to 14-membered non-aromatic heterocyclic group, a C₆₋₁₄

aromatic hydrocarbocyclic group or a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the following substituent group b.

The substituent group a: the group consisting of hydroxy group, a halogen atom and cyano group

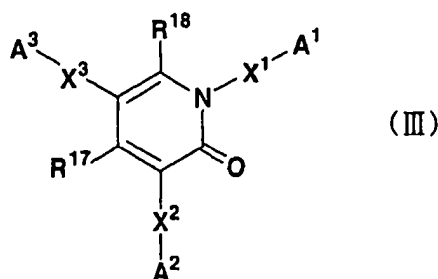
5 The substituent group b: the group consisting of (1) hydroxy group, (2) a halogen atom, (3) nitrile group, (4) nitro group, (5) a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group or a C₂₋₆ alkynyl group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆alkylamino group, a di-(C₁₋₆ alkyl)amino group, a C₂₋₆ alkenylamino group, a di(C₂₋₆ alkenylamino) group, a C₂₋₆ alkynylamino group, a di(C₂₋₆ alkynylamino) group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group, an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, an aralkyloxy group, a TB-
10 DMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group, a C₂₋₆ alkenylcarbonyloxy group, a C₂₋₆ alkynylcarbonyloxy group, an N-C₁₋₆ alkylcarbonyloxy group, an N-C₂₋₆ alkenylcarbonyloxy group and an N-C₁₋₆ alkynylcarbonyloxy group, (6) a C₁₋₆ alkoxy group, a C₂₋₆ alkenyloxy group or a C₂₋₆ alkynyloxy group which may be optionally substituted respectively with one or more groups selected from the group consisting of a C₁₋₆ alkylami-
15 no group, an aralkyloxy group and hydroxy group, (7) a C₁₋₆ alkylthio group, a C₂₋₆ alkenylthio group or a C₂₋₆ alkynylthio group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, nitrile group, a halogen atom, a C₁₋₆ alkylamino group, an aralkyloxy group, a TBDMS oxy group, a C₁₋₆ alkylsulfonylamino group, a C₁₋₆ alkylcarbonyloxy group and a C₁₋₆ alkylcarbonyloxy group, (8) a carbonyl group substituted with a group selected from the group consisting of a C₁₋₆ alkoxy group, amino group, a C₁₋₆ alkylamino group, a di(C₁₋₆ alkyl)amino group, a C₂₋₆ alkenylamino group, a di(C₂₋₆ alkenyl)amino group, a C₂₋₆ alkynylamino group, a di(C₂₋₆ alkynyl)amino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkenylamino group, an N-C₁₋₆ alkyl-N-C₂₋₆ alkynylamino group and an N-C₂₋₆ alkenyl-N-C₂₋₆ alkynylamino group, (9) amino group which may be optionally substituted with one or two groups selected from the group consisting of a C₁₋₆ alkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₁₋₆ alkylsulfonyl group, a C₂₋₆ alkenylsulfonyl group, a C₂₋₆ alkynylsulfonyl group, a C₁₋₆ alkylcarbonyl group, a C₂₋₆ alkenylcarbonyl group and a C₂₋₆ alkynylcarbonyl group, (10) a C₁₋₆ alkylsulfonyl group, (11) a C₂₋₆ alkenylsulfonyl group, (12) a C₂₋₆ alkynylsulfonyl group, (13) a C₁₋₆ alkylsulfinyl group, (14) a C₂₋₆ alkenylsulfinyl group, (15) a C₂₋₆ alkynylsulfinyl group, (16) a formyl group, (17) a C₃₋₈ cycloalkyl group or a C₃₋₈ cycloalkenyl group which may be optionally substituted respectively with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (18) a 5-to 14-membered non-aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, (19) a C₆₋₁₄ aromatic hydrocarbocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group, and (20) a 5- to 14-membered aromatic heterocyclic group which may be optionally substituted with one or more groups selected from the group consisting of hydroxy group, a halogen atom, nitrile group, a C₁₋₆ alkyl group, a C₁₋₆ alkyloxy group, a C₁₋₆ alkyloxy C₁₋₆ alkyl group and an aralkyl group.

- 40 4. The compound according to Claim 2, a salt thereof or hydrates thereof, wherein at least one of A¹, A² and A³ are the same as or different from each other and each is an optionally substituted C₃₋₈ cycloalkyl, C₃₋₈ cycloalkenyl or 5- to 14-membered non-aromatic heteroring.
- 45 5. The compound according to Claim 2, a salt thereof or hydrates thereof, wherein at least one of A¹, A² and A³ are the same as or different from each other and each is an optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or a 5- to 14-membered aromatic heteroring.
- 50 6. The compound according to claim 2, a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each represents phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, isoquinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group or morpholyl group which may optionally have a substituent, respectively.
- 55 7. The compound according to Claim 2, a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each is a group represented by the formula:



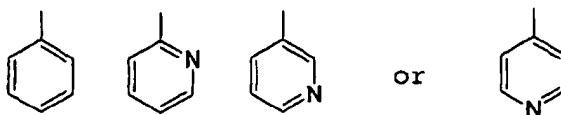
which may be substituted.

- 25
- 30
- 35
- 40
- 45
- 50
- 55
8. The compound according to Claim 2, a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each is optionally substituted with hydroxyl group, a halogen atom, amino group or nitrile group.
 9. The compound according to Claim 7, a salt thereof or hydrates thereof, wherein the substituents of A¹, A² and A³ are the same as or different from each other and each is hydroxyl group, a halogen atom or, amino group, nitrile group or nitro group.
 10. The compound according to Claim 1 or 2, a salt thereof or hydrates thereof, wherein Q is oxygen.
 11. The compound according to Claim 1 or 2, a salt thereof, hydrates thereof, wherein X¹, X² and X³ are the same as or different from each other and each represents single bond, -CH₂-, -CH(OH)-, -CH₂-CH₂-, -CH=CH-, -C≡C-, -O- or -CO-.
 12. The compound according to Claim 2, a salt thereof or hydrates thereof, wherein X¹, X² and X³ are single bonds.
 13. The compound according to Claim 2, a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ are the same as or different from each other and each represents hydrogen atom, fluorine, chlorine, bromine, iodine, methyl group, ethyl group, n-propyl group or iso-propyl group.
 14. The compound according to Claim 2, a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ represent hydrogen atom.
 15. The compound as claimed in Claim 1 or 2, a salt thereof or hydrates thereof, which is represented by the formula:



wherein X¹, X², X³, A¹, A², A³, R¹⁷ and R¹⁸ have the same meanings as defined in the above Claim 2.

- 15 16. The compound according to Claim 15, a salt thereof or hydrates thereof, wherein A¹, A² and A³ are same as or different from each other and each represents optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or 5- to 14-membered aromatic heteroring.
- 20 17. The compound according to Claim 15, a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each represents optionally substituted phenyl group, pyrrolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group, carbazolyl group, cyclopentyl group, cyclohexyl group, cyclohexenyl group, dioxinyl group, adamantyl group, pyrrolidinyl group, piperidinyl group, piperazinyl group or morpholyl group.
- 25 18. The compound according to claim 15, a salt thereof or hydrates thereof, wherein A¹, A² and A³ are the same as or different from each other and each represents a group represented by the following formula:



which may be substituted.

- 40 19. The compound according to Claim 15, a salt thereof or hydrates thereof, wherein the bonding site of the substituent at A¹, A² and/or A³ are α -position of the carbon atom bonding to the group X¹, X² and X³, respectively.
20. The compound according to Claim 15, a salt thereof or hydrates thereof, wherein X¹, X² and X³ are single bonds.
- 45 21. The compound according to Claim 15, a salt thereof or hydrates thereof, wherein R¹⁷ and R¹⁸ are hydrogen atoms.
- 50 22. The compound according to Claim 1, a salt thereof or hydrates thereof, which is any one of compounds selected from: 3-(2-cyanophenyl)-5-(2-methylsulfonylamino-phenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chloro-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-nitrophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-aminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylsulfonylamino-phenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-dimethylaminophenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-[3-(5-methoxymethyl-2-oxazolidinon-3-yl)-phenyl]-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methoxycarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-methylaminocarbonylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyano-3-pyridyl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-hydroxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-chlorophenyl)-5-(2-pyridyl)-1-(4-dimethylaminoethoxyphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-formylphenyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(3-hydroxymethylphenyl)-1,2-dihydropyridin-2-
- 55

5

10

15

20

25

30

35

40

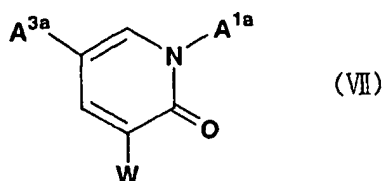
45

30

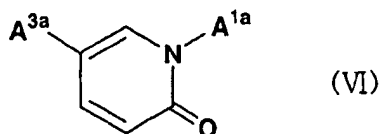
55

(2-cyanophenyl)-1-[3-(diisopropylaminoethoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(4-piperidinobutoxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(4-nitrophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-phenyl-5-(2-pyridyl)-3-(2-thiazolyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-pyridyl)-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-fluoropyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-cyanopyridin-3-yl)-1-phenyl-5-(2-pyrimidinyl)-1,2-dihydropyridin-2-one; 3-(2-nitrophenyl)-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-formylthiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-naphthyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(1-naphthyl)-1,2-dihydropyridin-2-one; 5-(2-aminopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 5-(2-bromopyridin-6-yl)-3-(2-cyanophenyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-morpholinopyridin-6-yl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-(3-hydroxyphenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-(4-piperidyloxy)phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-[3-(N-acetyl-piperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-1-[3-[1-(methanesulfonyl)piperidin-4-yl-oxy]phenyl]-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 1-[3-(N-methylpiperidin-4-yl-oxy)phenyl]-3-(2-cyanophenyl)-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-(6-chloro-1H-benzimidazol-2-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-(2-cyanophenyl)-5-(2-pyridyl)-1-(2-nitrotoluen-4-yl)-1,2-dihydropyridin-2-one; 3-(2-cyanothiophen-3-yl)-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)phenyl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; 3-[2-(5-oxazolyl)thiophen-3-yl]-1-phenyl-5-(2-pyridyl)-1,2-dihydropyridin-2-one; and 3-[(2-ethoxycarbonylvinyl)thiophen-3-yl]-5-(2-pyridyl)-1-phenyl-1,2-dihydropyridin-2-one.

23. A process for producing a compound represented by the formula:

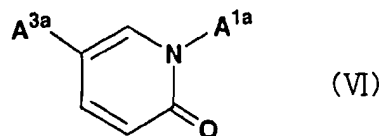


(wherein, each A^{1a} and A^{3a} has the same meaning as defined below; and W represents a halogen atom) or a salt thereof, which comprises subjecting the compound represented by the formula:



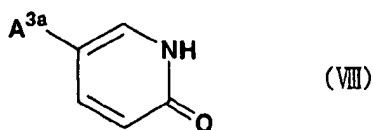
(wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates an optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group) or a salt thereof to a halogenation reaction.

24. A process for producing a compound represented by the formula:



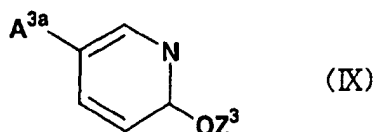
(wherein A^{1a} and A^{3a} have the same meanings as defined above) or a salt thereof, which comprises subjecting

the compound represented by the formula:



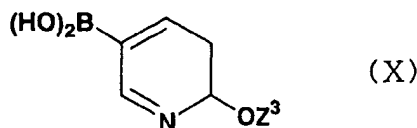
10 (wherein A^{3a} has the same meaning as defined above) or a salt thereof and a boronic acid derivative represented by the formula A^{1a}B(OH)₂ (wherein A^{1a} represents optionally substituted C₆₋₁₄ aromatic hydrocarbon ring or 5- to 14-membered aromatic heteroring) to a coupling reaction in the presence of a copper compound.

15 25. The production process according to Claim 24, which comprises subjecting the compound represented by the above formula (VIII) or a salt thereof produced by subjecting the compound represented by the formula:



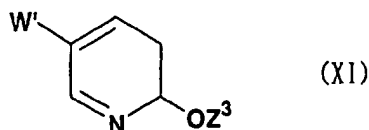
25 (wherein A^{3a} has the same meaning as defined above; and Z³ indicates a protecting group of an alcoholic hydroxy group) to de-protecting reaction and a boronic acid derivative represented by the formula A^{1a}B(OH)₂ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound.

30 26. The production process according to Claim 24, which comprises producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound represented by the above formula (IX) or a salt thereof produced by subjecting a boronic acid derivative represented by the formula:



40 (wherein Z³ has the same meaning as defined above) or a salt thereof and the compound represented by the formula A^{3a}·Z¹ (wherein A^{3a} has the same meaning as defined above; and Z¹ represents a halogen atom) or a salt thereof to a coupling reaction in the presence of a palladium catalyst, to a de-protecting reaction; and then subjecting the compound (VIII) or a salt thereof and a boronic acid derivative represented by the formula A^{1a}B(OH)₂ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound.

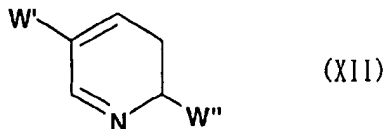
45 27. The production process according to Claim 24, which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the formula:



55 (wherein Z³ has the same meaning as defined above; and W' represents a halogen atom) or a salt thereof and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX) or a

salt thereof by subjecting the compound (X) or a salt and the compound represented by the formula $A^{3a}\text{-}Z^1$ (wherein A^{3a} and Z^1 have the same meanings as defined above) or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX) or a salt thereof to a de-protecting reaction; and then subjecting the compound (VIII) and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound.

28. The production process according to Claim 24, which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the above formula (XI) or a salt thereof produced by reacting the compound represented by the formula:



(wherein W' and W'' are the same as or different from each other and each represents halogen atoms) or a salt thereof and the compound represented by the formula Z^3OM (wherein Z^3 has the same meaning as defined above; and M represents an alkali metal atom) and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX) or a salt thereof by subjecting the compound (X) or a salt thereof and the compound represented by the formula $A^{3a}\text{-}Z^1$ (wherein A^{3a} and Z^1 have the same meanings as defined above) or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII) or a salt thereof by subjecting the compound (IX) or a salt thereof to a de-protecting reaction; and then subjecting the compound (VIII) and a boronic acid derivative represented by the formula $A^{1a}B(OH)_2$ (wherein A^{1a} has the same meaning as defined above) to a coupling reaction in the presence of a copper compound.

29. The production process according to Claim 23, which comprises subjecting the compound represented by the above formula (VI) and produced by the production process according to any of Claims 24 to 28 or a salt thereof to a halogenation reaction:

30. The production process according to Claim 23 or 29, wherein W is bromine or iodine.

31. The production process according to Claim 23 or 29, wherein the halogenation reaction for producing the compound (VII) or a salt thereof is (1) a bromination reaction using N -bromosuccinimide or acetic acid-bromine or (2) an iodination reaction using N -iodosuccinimide or iodine.

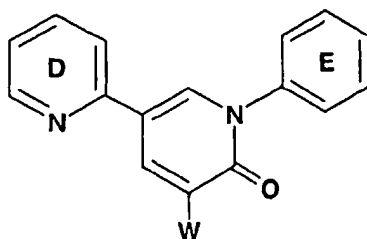
32. The production process according to Claim 23 or 29, wherein the halogenation reaction for producing the compound (VII) or a salt thereof is carried out using N,N -dimethylformamide as a solvent.

33. The production process according to Claim 23 or 29, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group.

34. The production process according to any of Claims 24 to 28, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group.

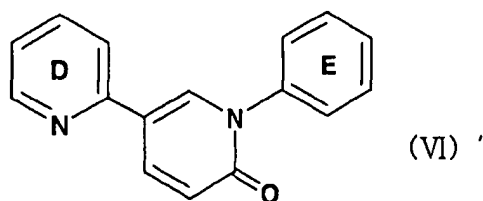
35. The production process according to any of Claims 24 to 29, wherein the copper compound used for a coupling reaction using the compound (VIII) or a salt thereof is copper acetate or di- μ -hydroxo-bis[(N,N,N',N' -tetramethylethylenediamine)copper (II)] chloride.

36. The production process according to any of Claims 24 to 29, wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out in the presence of a base.
37. The production process according to Claim 36, wherein the base is triethylamine, pyridine or tetramethyldiamine.
38. The production process according to any of Claims 24 to 29, wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent.
39. The production process according to any of Claims 25 to 29, wherein Z^3 is a C_{1-6} alkyl group or a C_{1-6} aralkyl group.
40. The production process according to claims 25 to 29, wherein the reaction of de-protection of the compound (IX) or a salt thereof is carried out in the presence of an acid.
41. The production process according to Claim 40, wherein the acid is hydrochloric acid.
42. The production process according to Claims 26 to 29, wherein a catalyst in the coupling reaction using the compound (X) or a salt thereof is palladium acetate and triphenylphosphine.
43. The production process according to Claims 26 to 29, wherein the coupling reaction using the compound (X) or a salt thereof is carried out in the presence of a base.
44. The production process according to Claim 43, wherein the base is cesium carbonate, sodium carbonate or potassium carbonate.
45. The production process according to any of Claims 27 to 29, wherein W' is bromine.
46. The production process according to Claims 27 to 29, wherein the base used for the reaction of the compound (XI) or a salt thereof with trimethoxyborane is n-butyllithium.
47. The production process according to Claim 28 or 29, wherein W' and W'' are bromine.
48. The production process according to Claim 28 or 29, wherein the compound represented by the formula Z^3OM is sodium methoxide or sodium ethoxide.
49. A process for producing a compound represented by the formula:



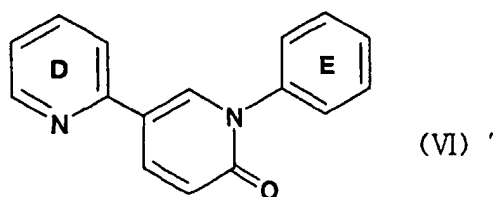
(VII)

(wherein, the ring D and the ring E have the same meanings as defined below; and W has the same meanings as defined above) or a salt thereof, which comprises subjecting a compound represented by the formula:

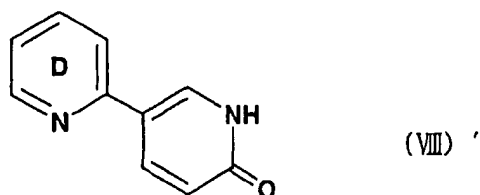


10 (wherein, the ring D ring indicates an optionally substituted pyridine ring; and the ring E represents an optionally substituted benzene ring) or a salt thereof to a halogenation reaction.

15 50. A process for producing a compound represented by the formula:

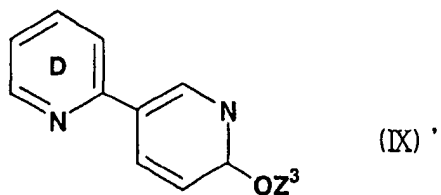


25 (wherein, the ring D and the ring E have the same meanings as defined above) or a salt thereof, which comprises subjecting the compound represented by the formula:



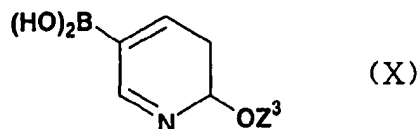
35 (wherein the ring D has the same meaning as defined above) or a salt thereof and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph indicates an optionally substituted phenyl group) to a coupling reaction in the presence of a copper compound.

40 51. The production process according to Claim 50, which comprises subjecting the compound represented by the above formula (VIII)' or a salt thereof produced by subjecting the compound represented by the formula:



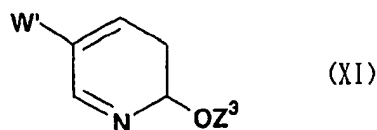
50 (wherein the ring B and Z^3 have the same meanings as defined above) or a salt thereof to a de-protecting reaction, and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound.

52. The production process according to claim 50, which comprises producing the compound represented by the above formula (VII)' or a salt thereof by subjecting the compound represented by the above formula (IX)' or a salt thereof produced by subjecting a boronic acid derivative represented by the formula:



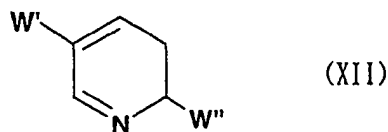
15 (wherein Z^3 has the same meaning as defined above) or a salt thereof and an optionally substituted 2-halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst to a de-protecting reaction; and then subjecting the compound (VIII)' or a salt thereof and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound.

- 20 53. The production process according to Claim 50, which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the formula:



30 (wherein Z^3 has the same meaning as defined above; and W' represents a halogen atom) or a salt thereof and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX)' or a salt thereof by subjecting the compound (X) or a salt thereof and an optionally substituted 2-halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII)' or a salt thereof by subjecting the compound (IX)' or a salt to a de-protecting reaction; and then subjecting the compound (VIII)' and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) in the presence of a copper compound.

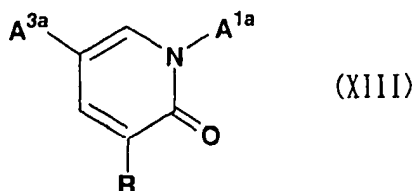
- 40 54. The production process according to Claim 50, which comprises producing the compound represented by the above formula (X) or a salt thereof by reacting the compound represented by the above formula (XI) or a salt thereof produced by reacting the compound represented by the formula:



50 (wherein W' and W'' are the same as or different from each other and each represents halogen atoms) or a salt thereof and the compound represented by the formula $Z^3\text{OM}$ (wherein Z^3 and M have the same meanings as defined above), and trimethoxyborane in the presence of a base; producing the compound represented by the above formula (IX)' or a salt thereof by subjecting the compound (X) or a salt and an optionally substituted 2-halogenopyridine or a salt thereof to a coupling reaction in the presence of a palladium catalyst; producing the compound represented by the above formula (VIII)' or a salt thereof by subjecting the compound (IX)' or a salt to a de-protecting reaction; and then subjecting the compound (VIII)' and a boronic acid derivative represented by the formula $\text{PhB}(\text{OH})_2$ (wherein Ph has the same meaning as defined above) to a coupling reaction in the presence of a copper compound.

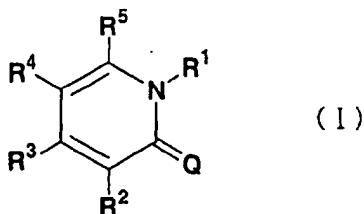
55. The production process according to Claim 25, which comprises subjecting the compound represented by the above formula (VI)' and produced by the production process according to any of Claims 29 to 32 or a salt thereof to a halogenation reaction.
- 5 56. The production process according to Claim 49 or 55, wherein W is bromine or iodine.
57. The production process according to claim 49 or 55, wherein the halogenation reaction for producing the compound (VII) or a salt thereof is (1) a bromination reaction using N-bromosuccinimide or acetic acid-bromine, or (2) an iodination reaction using N-iodosuccinimide or iodine.
- 10 58. The production process according to Claim 49 or 55, wherein the halogenation reaction for producing the compound (VII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent.
- 15 59. The production process according to Claim 49 or 55, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group.
- 20 60. The production process according to any of Claims 50 to 54, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, iso-quinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group.
- 25 61. The production process according to any of Claims 50 to 55, wherein the copper compound used for the coupling reaction using the compound (VIII) or a salt thereof is copper acetate or di-μ-hydroxo-bis[(N,N,N',N'-tetramethylethylenediamine)copper (II)] chloride.
- 30 62. The production process according to any of Claims 50 to 55, wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out in the presence of a base.
63. The production process according to claim 62, wherein the base is triethylamine, pyridine or tetramethylenediamine.
- 35 64. The production process according to any of Claims 50 to 55, wherein the coupling reaction using the compound (VIII) or a salt thereof is carried out using N,N-dimethylformamide as a solvent.
65. The production process according to any of Claims 51 to 55, wherein Z³ is a C₁₋₆ alkyl group or an aralkyl group.
- 40 66. The production process according to Claims 51 to 55, wherein the de-protection reaction of the compound (IX) or a salt thereof is carried out in the presence of an acid.
67. The production process according to Claim 66, wherein the acid is hydrochloric acid.
- 45 68. The production process according to Claims 52 to 55, wherein a catalyst in the coupling reaction using the compound (X) or a salt thereof is palladium acetate and triphenylphosphine.
69. The production process according to Claims 52 to 55, wherein the coupling reaction using the compound (X) or a salt thereof is carried out in the presence of a base.
- 50 70. The production process according to Claim 69, wherein the base is cesium carbonate, sodium carbonate or potassium carbonate.
71. The production process according to any of Claims 53 to 55, wherein W' is bromine.
- 55 72. The production process according to Claims 53 to 55, wherein the base used for the reaction of the compound (XI) or a salt thereof with trimethoxyborane is n-butyllithium.

73. The production process according to Claim 54 to 55, wherein W' and W'' are bromine.
74. The production process according to Claim 54 or 55, wherein the compound represented by the formula Z³OM is sodium methoxide or sodium ethoxide.
75. The production process according to any of Claims 52 to 55, wherein the optionally substituted 2-halogenopyridine is an optionally substituted 2-bromopyridine.
76. A compound represented by the following formula, a salt thereof or hydrates thereof.



Wherein A^{1a} and A^{3a} are the same as or different from each other and each indicates optionally substituted C₆₋₁₄ aromatic hydrocarbocyclic group or 5 to 14-membered aromatic heterocyclic group; and R indicates hydrogen atom or a halogen atom.

77. The compound according to Claim 76, a salt thereof or hydrates thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, thienyl group, thiazolyl group, furyl group, naphthyl group, quinolyl group, isoquinolyl group, indolyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, imidazopyridyl group or carbazolyl group.
78. The compound according to Claim 76, a salt thereof or hydrates thereof, wherein A^{1a} and A^{3a} are the same as or different from each other and each represents optionally substituted phenyl group, pyridyl group, pyrimidinyl group, thienyl group or furyl group.
79. The compound according to claim 76, a salt thereof or hydrates thereof, wherein R is hydrogen atom or bromine.
80. A pharmaceutical composition comprising a compound represented by the following formula, a salt thereof or hydrates thereof.



In the formula, Q indicates NH, O or S; and R¹, R², R³, R⁴ and R⁵ are the same as or different from each other and each indicates hydrogen atom, a halogen atom, a C₁₋₆ alkyl group or the formula -X-A (wherein X indicates a single bond, a C₁₋₆ alkylene group which may optionally have substituents, a C₂₋₆ alkenylene group which may optionally have substituents, a C₂₋₆ alkynylene group which may optionally have substituents, -O-, -S-, -CO-, -SO-, -SO₂-, -N(R⁶)-, -N(R⁷)-CO-, -CO-N(R⁸)-, -N(R⁹)-CH₂-, -CH₂-N(R¹⁰)-, -CH₂-CO-, -CO-CH₂-, -N(R¹¹)-S(O)_m-, -S(O)_n-N(R¹²)-, -CH₂-S(O)_p-, -S(O)_q-CH₂-, -CH₂-O-, -O-CH₂-, -N(R¹³)-CO-N(R¹⁴)- or -N(R¹⁵)-CS-N(R¹⁶)- (wherein R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵ and R¹⁶ indicates hydrogen atom, a C₁₋₆ alkyl group or a C₁₋₆ alkoxy group; and m, n, p and q are independent of each other and each indicates an integer of 0, 1 or 2); and A indicates

EP 1 300 396 A1

optionally substituted C₃₋₈ cycloalkyl group, C₃₋₈ cycloalkenyl group, 5- to 14-membered non-aromatic heterocyclic group, C₆₋₁₄ aromatic hydrocarbocyclic group or 5-to 14-membered aromatic heterocyclic group), provided that 3 groups among R¹, R², R³, R⁴ and R⁵ are always the same as or different from each other and each indicates -X-A; and the residual 2 groups always indicate hydrogen atom, a halogen atom or a C₁₋₆ alkyl group.

- 5 81. The pharmaceutical composition according to Claim 80, wherein it is an inhibitor to an α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (hereinafter, referred to as "AMPA") receptor and/or a kainate receptor.
- 10 82. The pharmaceutical composition according to Claim 80, wherein it is an inhibitor to an AMPA receptor.
83. The pharmaceutical composition according to Claim 80, wherein it is an inhibitor to a kainate receptor.
- 15 84. The pharmaceutical composition according to Claim 80, which is a therapeutic or preventive agent for the diseases in which an AMPA receptor or a kainate receptor is participated.
85. The pharmaceutical composition according to Claim 80, which is a therapeutic or preventive agent for the diseases in which a kainate receptor is participated.
- 20 86. The pharmaceutical composition according to Claim 80, which is a therapeutic or preventive agent for acute neurodegenerative disease.
87. The pharmaceutical composition according to Claim 80, which is a therapeutic or preventive agent for cerebrovascular disorders at acute stage, head injury, spinal cord injury, neuropathies caused by hypoxia or hypoglycemia.
- 25 88. The pharmaceutical composition according to Claim 80, which is a therapeutic or preventive agent for chronic neurodegenerative disease.
- 30 89. The pharmaceutical composition according to Claim 80, which is a therapeutic or preventive agent for Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis or spinocerebellar degeneration.
90. The pharmaceutical composition according to Claim 80, which is an agent for treating or preventing epilepsy, hepatic encephalopathy, peripheral neuropathy, Parkinson's syndrome, spasticity, pain, neuralgia, schizophrenia, anxiety, drug abuse, nausea, emesis, dysuria, paropsia caused by glaucoma, paraculis caused by antibiotics or food poisoning.
- 35 91. The pharmaceutical composition according to Claim 80, which is an agent for treating or preventing infectious encephalomyelitis, cerebrovascular senile dementia, or dementia or neurosis caused by cerebrospinal meningitis.
- 40 92. The pharmaceutical composition according to Claim 91, wherein the infectious encephalomyelitis is HIV encephalomyelitis.
93. The pharmaceutical composition according to Claim 80, which is an agent for treating or preventing demyelinating disease.
- 45 94. The pharmaceutical composition according to Claim 93, wherein the demyelinating disease is encephalitis, acute disseminated encephalomyelitis, multiple sclerosis, acute demyelinating polyneuropathy, Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, Marchifava-Bignami disease, central pontine myelinolysis, neuromyelitis optica, Devic disease, Balo disease, HIV myelopathy, HTLV myelopathy, progressive multifocal leukoencephalopathy or secondary demyelinating disease.
- 50 95. The pharmaceutical composition according to Claim 94, wherein the secondary demyelinating disease is CNS lupus erythematoses, polyarteritis nodosa, Sjogren's syndrome, sarcoidosis or isolated cerebral vasculitis.
- 55 96. A process for preventing or treating diseases in which AMPA receptor or kainate receptor is participated, by dosing a pharmacologically effective dose of the compound represented by the formula (I), a salt thereof or hydrates thereof to a patient.
97. The method according to Claim 96, wherein the diseases are acute neurodegenerative disease, cerebrovascular

disorders at acute stage, head injury, spinal cord injury, neuropathies caused by hypoxia or hypoglycemia, chronic neurodegenerative disease, Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis, spinocerebellar degeneration, epilepsy, hepatic encephalopathy, peripheral neuropathy, Parkinson's syndrome, spasticity, pain, neuralgia, schizophrenia, anxiety, drug abuse, nausea, emesis, dysuria, paropsia caused by glaucoma, paracsis caused by antibiotics, food poisoning, the infectious encephalomyelitis comprising HIV encephalomyelitis, cerebrovascular senile dementia, dementia or neurosis caused by cerebrospinal meningitis, or demyelinating diseases such as encephalitis; acute disseminated encephalomyelitis; multiple sclerosis; acute demyelinating polyneuropathy; Guillain-Barre syndrome; chronic inflammatory demyelinating polyneuropathy; Marchifava-Bignami disease; central pontine myelinolysis; neuromyelitis optica; Devic disease; Baló disease; HIV myelopathy; HTLV myelopathy; progressive multifocal leukoencephalopathy; and the secondary demyelinating diseases such as CNS lupus erythematosus; polyarteritis nodosa; Sjögren syndrome; sarcoidosis and isolated cerebral vasculitis.

98. Use of the compound represented by the formula (I), a salt thereof or hydrates thereof for producing a therapeutic or preventive agent for diseases in which AMPA receptor or kainate receptor is participated.

99. The use according to Claim 98, wherein the diseases are acute neurodegenerative disease, cerebrovascular disorders at acute stage, head injury, spinal cord injury, neuropathies caused by hypoxia or hypoglycemia, chronic neurodegenerative disease, Alzheimer's disease, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis, spinocerebellar degeneration, epilepsy, hepatic encephalopathy, peripheral neuropathy, Parkinson's syndrome, spasticity, pain, neuralgia, schizophrenia, anxiety, drug abuse, nausea, emesis, dysuria, paropsia caused by glaucoma, paracsis caused by antibiotics, food poisoning, the infectious encephalomyelitis comprising HIV encephalomyelitis, cerebrovascular senile dementia, dementia or neurosis caused by cerebrospinal meningitis, or demyelinating diseases such as encephalitis; acute disseminated encephalomyelitis; multiple sclerosis; acute demyelinating polyneuropathy; Guillain-Barre syndrome; chronic inflammatory demyelinating polyneuropathy; Marchifava-Bignami disease; central pontine myelinolysis; neuromyelitis optica; Devic disease; Baló disease; HIV myelopathy; HTLV myelopathy; progressive multifocal leukoencephalopathy; and the secondary demyelinating diseases such as CNS lupus erythematosus; polyarteritis nodosa; Sjögren's syndrome; sarcoidosis and isolated cerebral vasculitis.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP01/04857

A. CLASSIFICATION OF SUBJECT MATTER Int.Cl. ⁷ C07D213/64, 71, 74, 82, 84, 89, 401/04, 14, 405/04, 14, 409/04, 14, 413/14, 417/04, 14, 471/04, A61K31/44, 443, 4433, 4436, 4439, 444, 4545, 4709, 4725, 496, 501, 5377, A61P43/00, 25/00, 9/10, 25/14, 16, 28, 21/04, 25/02, 04, 08, 18, 22, 30, 1/08, 13/02 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) Int.Cl. ⁷ C07D213/00-89, 401/00-14, 405/00-14, 409/00-14, 413/00-14, 417/00-14, 471/00-04, A61K31/00-5377 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) REGISTRY (STN), CAPLUS (STN)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/31062 A1 (Shionogi & Co., Ltd.), 24 June, 1999 (24.06.99), especially, description, page 122, working example 445, etc. & AU 9915045 A1	1-11, 13-18, 21 23-95, 98-99
A		
X	WO 98/50384 A1 (Merck Sharp & Dohme Ltd.), 12 November, 1998 (12.11.98), especially, description, pages 22, example 1, step 3, etc. & EP 980371 A1 & US 6133255 A	1-11, 13-18, 21 23-95, 98-99
A		
X	WO 96/33974 A1 (The Green Cross Corporation), 31 October, 1996 (31.10.96), especially, working examples 11 to 15, 70 to 73, etc. & EP 826671 A1 & US 5948785 A	1-11, 13-18, 21 23-95, 98-99
A		
X	NADIN, A., HARRISON, T., "Synthesis of tricyclic pyridones by radical cyclization", Tetrahedron Letters, (1999), Vol.40, No.21, pages 4073 to 4076 especially, page 4047, chemical compounds 9(a) to 9(e), etc.	1-11, 13-18, 21 23-95, 98-99
A		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 20 August, 2001 (20.08.01)		Date of mailing of the international search report 11 September, 2001 (11.09.01)
Name and mailing address of the ISA/ Japanese Patent Office		Authorized officer
Facsimile No.		Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP01/04857

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	FUJITA, R., TOMISAWA, H., "Studies on 1-alkyl-2(1H)-pyridone derivatives. XXXII. The Friedel-Crafts reaction of 1-alkyl-2(1H)-pyridone derivatives with acid anhydride", Yakugaku Zasshi, (1990), Vol.110, No.6, pages 449 to 452 especially, page 450, compounds 1(a), 1(b), etc.	1-11, 13-19, 21 23-95, 98-99

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP01/04857

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 96,97
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 96 and 97 pertain to methods for treatment for human diseases by therapy as provided for in Rule 39.1(iv) of the Regulations under the PCT as a subject matter of international application which this International Searching Authority is not required to search.
2. ☒ Claims Nos.: 1-14,85-95,98,99
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claims 1-14, 85-95, 98, and 99 fail to be sufficiently supported by the description to such an extent that a meaningful search could not be carried out.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1992)